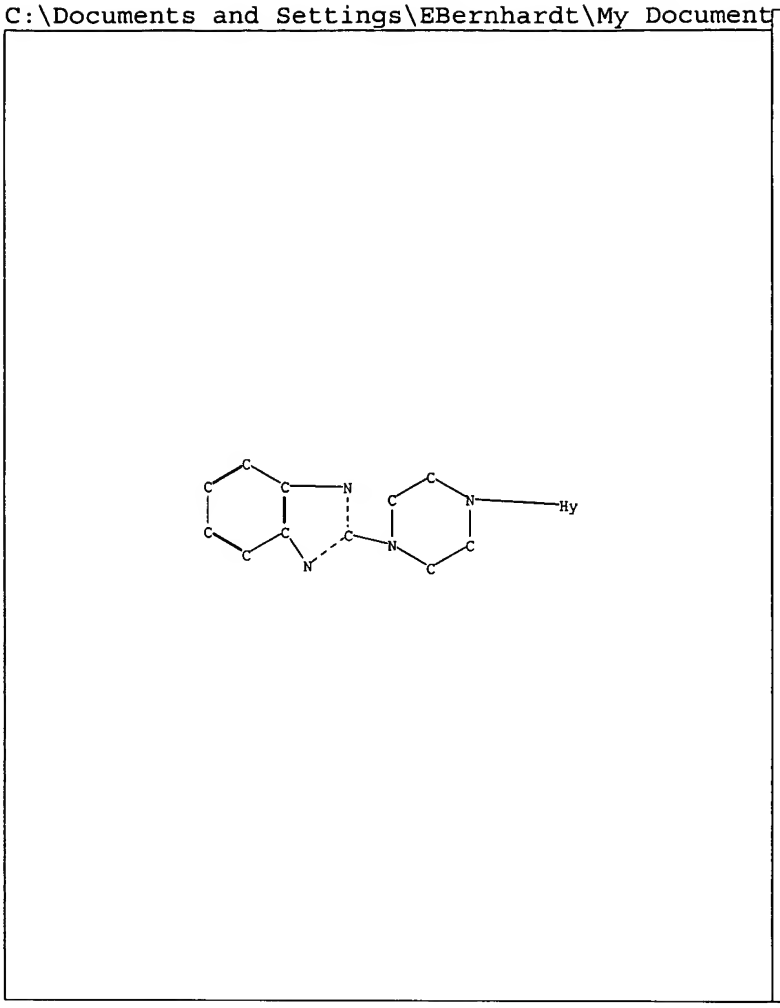
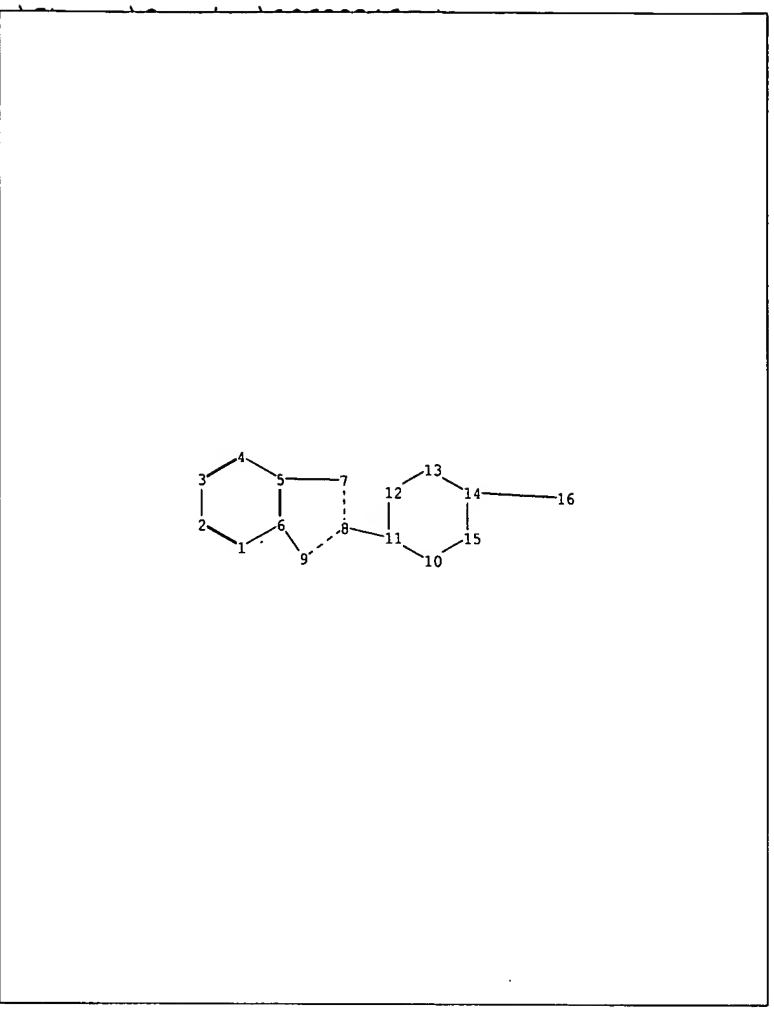
C:\Documents and Settings\EBernhardt\My Document

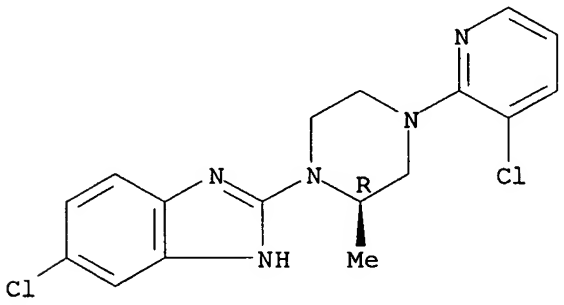




chain nodes :
    16
ring nodes :
    1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
chain bonds :
    8-11 14-16
ring bonds :
    1-2 1-6 2-3 3-4 4-5 5-6 5-7 6-9 7-8 8-9 10-11 10-15 11-12 12-13 13-14
    14-15
exact/norm bonds :
    5-7 6-9 7-8 8-9 8-11 10-11 10-15 11-12 12-13 13-14 14-15 14-16
normalized bonds :
    1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
    containing 1 : 10 :

Match level :
    1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom 11:Atom
    12:Atom 13:Atom 14:Atom 15:Atom 16:Atom

```
=> s l1
SAMPLE SEARCH INITIATED 12:53:05 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED -      277 TO ITERATE

100.0% PROCESSED      277 ITERATIONS                                  15 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS:  ONLINE  **COMPLETE**
                        BATCH   **COMPLETE**
PROJECTED ITERATIONS:          4542 TO     6538
PROJECTED ANSWERS:               68 TO      532

L2           15 SEA SSS SAM L1

=> d l2 1-15

L2   ANSWER 1 OF 15  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   722498-12-6  REGISTRY
ED   Entered STN:  05 Aug 2004
CN   1H-Benzimidazole, 5-chloro-2-[(2R)-4-(3-chloro-2-pyridinyl)-2-methyl-1-
     piperazinyl]- (9CI)  (CA INDEX NAME)
FS   STEREOSEARCH
MF   C17 H17 Cl2 N5
SR   CA
LC   STN Files:   CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry.
```

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**PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT**

              2 REFERENCES IN FILE CA (1907 TO DATE)
              2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2   ANSWER 2 OF 15  REGISTRY  COPYRIGHT 2006 ACS on STN
RN   722498-02-4  REGISTRY
ED   Entered STN:  05 Aug 2004
CN   1H-Benzimidazole, 2-[4-(3-chloro-2-pyridinyl)-1-piperazinyl]-1,5,6-
     trimethyl- (9CI)  (CA INDEX NAME)
FS   3D CONCORD
MF   C19 H22 Cl N5
SR   CA
LC   STN Files:   CA, CAPLUS, CASREACT, USPATFULL
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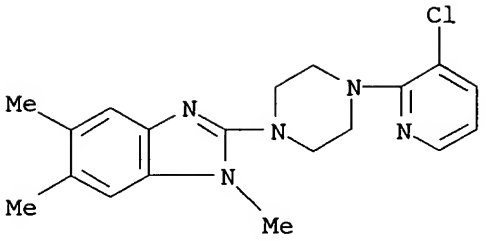
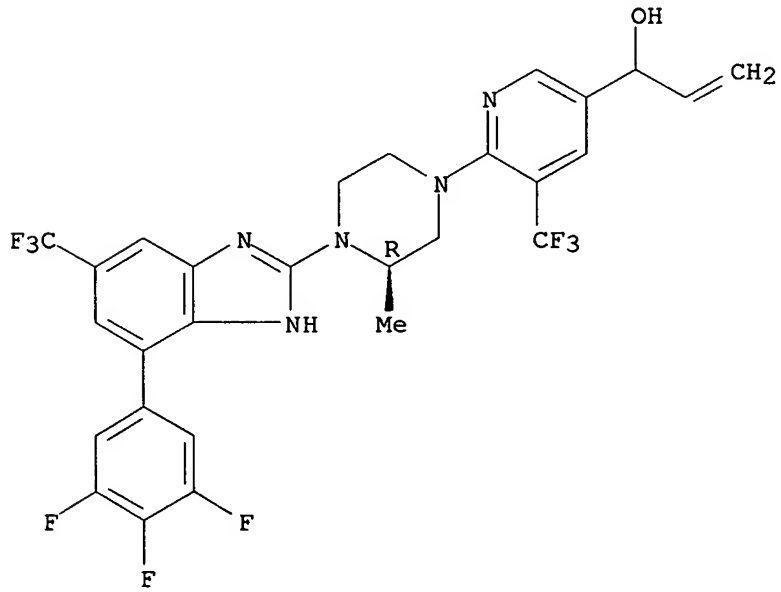


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1907 TO DATE)
2 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 3 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 683245-68-3 REGISTRY
ED Entered STN: 19 May 2004
CN 3-Pyridinemethanol, .alpha.-ethenyl-6-[(3R)-3-methyl-4-[6-(trifluoromethyl)-4-(3,4,5-trifluorophenyl)-1H-benzimidazol-2-yl]-1-piperazinyl]-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-[6-[(3R)-3-Methyl-4-[6-(trifluoromethyl)-4-(3,4,5-trifluorophenyl)-1H-benzimidazol-2-yl]piperazin-1-yl]-5-(trifluoromethyl)pyridin-3-yl]prop-2-en-1-ol
FS STEREOSEARCH
MF C28 H22 F9 N5 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.

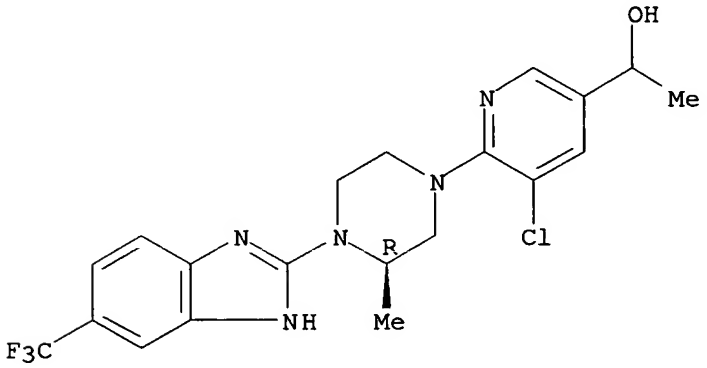


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 4 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 683245-60-5 REGISTRY
ED Entered STN: 19 May 2004
CN 3-Pyridinemethanol, 5-chloro-.alpha.-methyl-6-[(3R)-3-methyl-4-[5-(trifluoromethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 1-[5-Chloro-6-[(3R)-3-methyl-4-[6-(trifluoromethyl)-1H-benzimidazol-2-yl]piperazin-1-yl]pyridin-3-yl]ethanol
FS STEREOSEARCH
MF C20 H21 Cl F3 N5 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

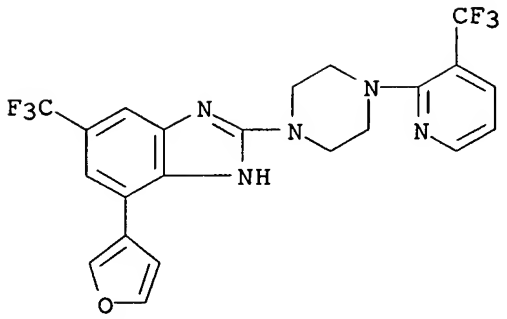
Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

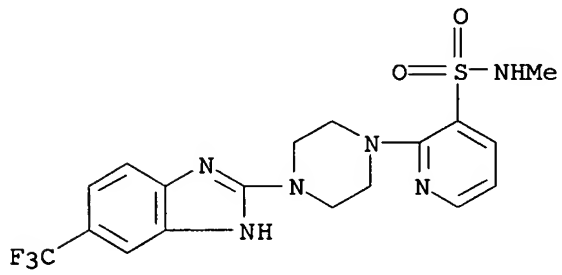
L2 ANSWER 5 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 683245-44-5 REGISTRY
ED Entered STN: 19 May 2004
CN 1H-Benzimidazole, 4-(3-furanyl)-6-(trifluoromethyl)-2-[4-[3-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C22 H17 F6 N5 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

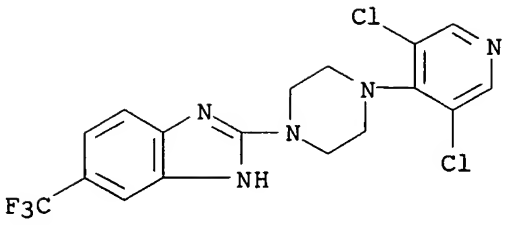
L2 ANSWER 6 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 683245-15-0 REGISTRY
ED Entered STN: 19 May 2004
CN 3-Pyridinesulfonamide, N-methyl-2-[4-[5-(trifluoromethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C18 H19 F3 N6 O2 S
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

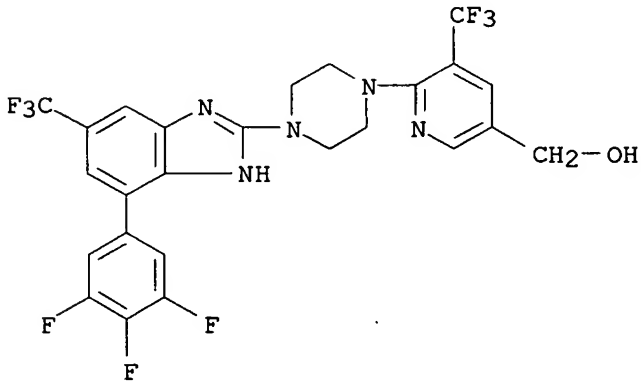
L2 ANSWER 7 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 683244-69-1 REGISTRY
ED Entered STN: 19 May 2004
CN 1H-Benzimidazole, 2-[4-(3,5-dichloro-4-pyridinyl)-1-piperazinyl]-5-(trifluoromethyl)- (9CI) (CA INDEX NAME)
FS 3D CONCORD
MF C17 H14 Cl2 F3 N5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 8 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 683244-46-4 REGISTRY
ED Entered STN: 19 May 2004
CN 3-Pyridinemethanol, 5-(trifluoromethyl)-6-[4-[6-(trifluoromethyl)-4-(3,4,5-trifluorophenyl)-1H-benzimidazol-2-yl]-1-piperazinyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN [5-Trifluoromethyl-6-[4-[5-trifluoromethyl-7-(3,4,5-trifluorophenyl)-1H-benzimidazol-2-yl]piperazin-1-yl]pyridin-3-yl]methanol
FS 3D CONCORD
MF C25 H18 F9 N5 O
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

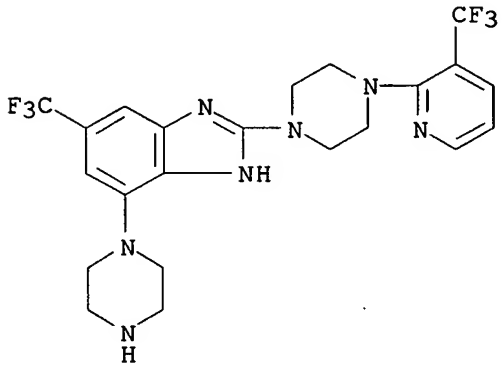


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 9 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 683243-72-3 REGISTRY
ED Entered STN: 19 May 2004
CN 1H-Benzimidazole, 4-(1-piperazinyl)-6-(trifluoromethyl)-2-[4-[3-

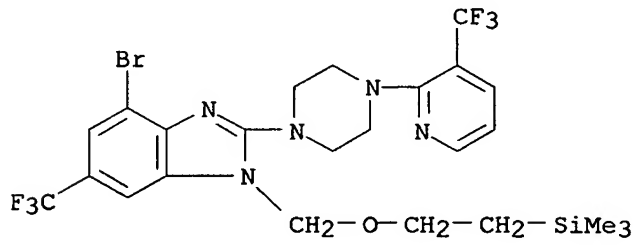
(trifluoromethyl)-2-pyridinyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-(Piperazin-1-yl)-6-trifluoromethyl-2-[4-(3-trifluoromethylpyridin-2-yl)piperazin-1-yl]-1H-benzimidazole
FS 3D CONCORD
MF C22 H23 F6 N7
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 10 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 683243-68-7 REGISTRY
ED Entered STN: 19 May 2004
CN 1H-Benzimidazole, 4-bromo-6-(trifluoromethyl)-2-[4-[3-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl]-1-[[2-(trimethylsilyl)ethoxy]methyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 4-Bromo-6-trifluoromethyl-2-[4-(3-trifluoromethylpyridin-2-yl)piperazin-1-yl]-1-[[2-(trimethylsilanyl)ethoxy]methyl]-1H-benzimidazole
FS 3D CONCORD
MF C24 H28 Br F6 N5 O Si
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

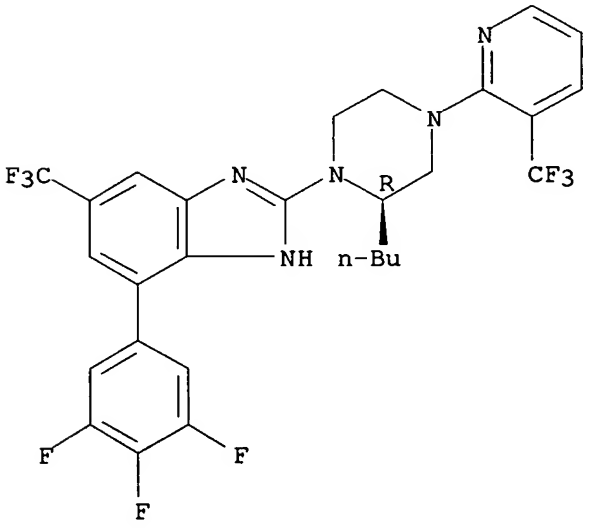
1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 11 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 683242-48-0 REGISTRY
ED Entered STN: 19 May 2004
CN 1H-Benzimidazole, 2-[(2R)-2-butyl-4-[3-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl]-6-(trifluoromethyl)-4-(3,4,5-trifluorophenyl)-, mono(trifluoroacetate) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2-[(2R)-2-Butyl-4-(3-trifluoromethylpyridin-2-yl)piperazin-1-yl]-5-trifluoromethyl-7-(3,4,5-trifluorophenyl)-1H-benzimidazole monotrifluoroacetate
FS STEREOSEARCH
MF C28 H24 F9 N5 . C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

CM 1

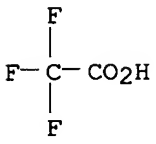
CRN 683242-47-9
CMF C28 H24 F9 N5

Absolute stereochemistry.



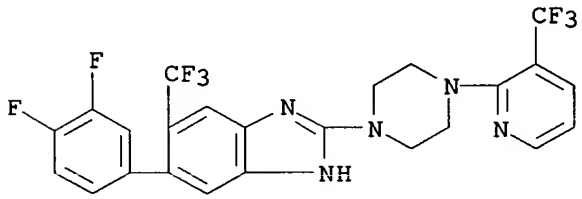
CM 2

CRN 76-05-1
CMF C2 H F3 O2



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 12 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 683241-89-6 REGISTRY
ED Entered STN: 19 May 2004
CN 1H-Benzimidazole, 5-(3,4-difluorophenyl)-6-(trifluoromethyl)-2-[4-[3-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 5-(3,4-Difluorophenyl)-6-trifluoromethyl-2-[4-(3-trifluoromethylpyridin-2-yl)piperazin-1-yl]-1H-benzimidazole
FS 3D CONCORD
MF C24 H17 F8 N5
SR CA
LC STN Files: CA, CAPLUS, USPATFULL



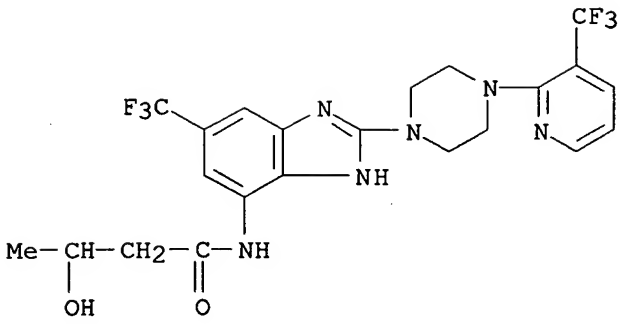
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 13 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 683241-53-4 REGISTRY
ED Entered STN: 19 May 2004
CN Butanamide, 3-hydroxy-N-[5-(trifluoromethyl)-2-[4-[3-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl]-1H-benzimidazol-7-yl]-, bis(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 3-Hydroxy-N-[5-(trifluoromethyl)-2-[4-[3-(trifluoromethyl)pyridin-2-yl]piperazin-1-yl]-1H-benzimidazol-7-yl]butanamide ditrifluoroacetate
MF C22 H22 F6 N6 O2 . 2 C2 H F3 O2
SR CA
LC STN Files: CA, CAPLUS, USPATFULL

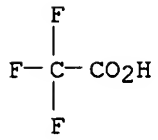
CM 1

CRN 683241-52-3
CMF C22 H22 F6 N6 O2



CM 2

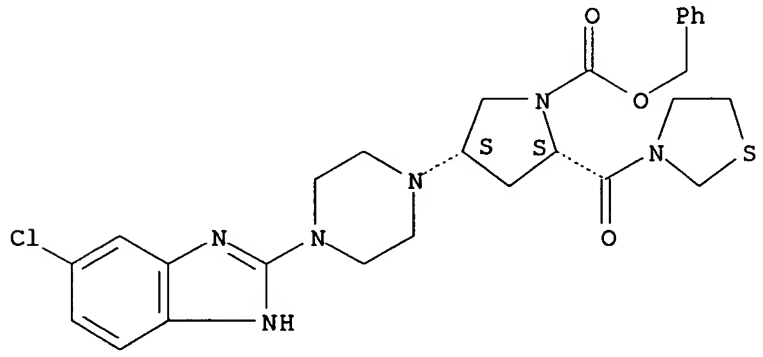
CRN 76-05-1
CMF C2 H F3 O2



1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 14 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 401567-04-2 REGISTRY
ED Entered STN: 17 Mar 2002
CN 1-Pyrrolidinecarboxylic acid, 4-[4-(5-chloro-1H-benzimidazol-2-yl)-1-piperazinyl]-2-(3-thiazolidinylcarbonyl)-, phenylmethyl ester, (2S,4S)-(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C27 H31 Cl N6 O3 S
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.

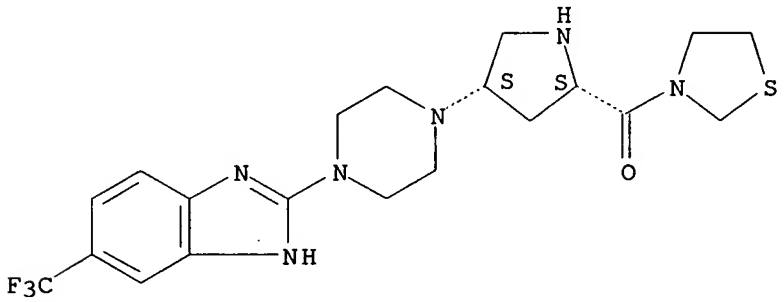


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

L2 ANSWER 15 OF 15 REGISTRY COPYRIGHT 2006 ACS on STN
RN 401563-27-7 REGISTRY
ED Entered STN: 17 Mar 2002
CN Thiazolidine, 3-[[(2S,4S)-4-[4-[5-(trifluoromethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, trihydrobromide (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C20 H25 F3 N6 O S . 3 Br H
SR CA
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL
CRN (790200-70-3)

Absolute stereochemistry.



●3 HBr

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

=> d his

(FILE 'HOME' ENTERED AT 12:50:53 ON 16 FEB 2006)

FILE 'REGISTRY' ENTERED AT 12:52:18 ON 16 FEB 2006
L1 STRUCTURE UPLOADED
L2 15 S L1

=> s l1 sss full
FULL SEARCH INITIATED 12:55:13 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 5644 TO ITERATE

100.0% PROCESSED 5644 ITERATIONS 429 ANSWERS
SEARCH TIME: 00.00.01

L3 429 SEA SSS FUL L1

=> save l3
ENTER NAME OR (END):ten688246/a
ANSWER SET L3 HAS BEEN SAVED AS 'TEN688246/A'

=> file caplus
COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION
FULL ESTIMATED COST | 197.64 | 198.06

FILE 'CAPLUS' ENTERED AT 12:55:38 ON 16 FEB 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 16 Feb 2006 VOL 144 ISS 8
FILE LAST UPDATED: 15 Feb 2006 (20060215/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

=> s l3
L4 19 L3

=> d l4 1-19 bib abs fhitstr

L4 ANSWER 1 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:1287372 CAPLUS
DN 144:100879
TI Proton activation does not alter antagonist interaction with the capsaicin-binding pocket of TRPV1
AU Gavva, Narender R.; Tamir, Rami; Klionsky, Lana; Norman, Mark H.; Louis, Jean-Claude; Wild, Kenneth D.; Treanor, James J. S.
CS Department of Neuroscience, Amgen Inc., Thousand Oaks, CA, USA
SO Molecular Pharmacology (2005), 68(6), 1524-1533
CODEN: MOPMA3; ISSN: 0026-895X
PB American Society for Pharmacology and Experimental Therapeutics
DT Journal
LA English
AB Vanilloid receptor 1 (TRPV1) is activated by chem. ligands (e.g., capsaicin and protons) and heat. In this study, the authors show that several compds. (AMG6880, AMG7472, and BCTC) are potent antagonists of rat TRPV1 activation by either capsaicin or protons (pH 5) (defined here as group A antagonists), whereas AMG0610, capsazepine, and SB-366791 are antagonists of capsaicin, but not proton, activation (defined here as group B antagonists). By using capsaicin-sensitive and insensitive rabbit

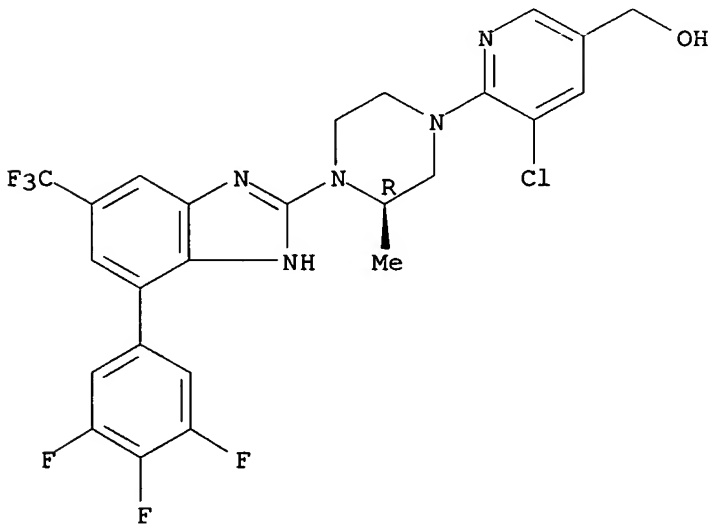
TRPV1 channels, the authors show that antagonists require the same crit. mol. determinants located in the transmembrane domain 3/4 region to block both capsaicin and proton activation, suggesting the presence of a single binding pocket. To det. whether the differential pharmacol. is a result of proton activation-induced conformational changes in the capsaicin-binding pocket that alter group B antagonist affinities, the authors have developed a functional antagonist competition assay. The authors hypothesized that if group B antagonists bind at the same or an overlapping binding pocket of TRPV1 as group A antagonists, and proton activation does not alter the binding pocket, then group B antagonists should compete with and prevent group A antagonism of TRPV1 activation by protons. Indeed, the authors found that each of the group B antagonists competed with and prevented BCTC, AMG6880 or AMG7472 antagonism of rat TRPV1 activation by protons with pA2 values similar to those for blocking capsaicin, indicating that proton activation does not alter the conformation of the TRPV1 capsaicin-binding pocket. In conclusion, group A antagonists seem to lock the channel conformation in the closed state, blocking both capsaicin and proton activation.

IT **683244-00-0**, AMG 7472
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(proton activation does not alter antagonist interaction with the capsaicin-binding pocket of TRPV1)

RN 683244-00-0 CAPLUS

CN 3-Pyridinemethanol, 5-chloro-6-[(3R)-3-methyl-4-[6-(trifluoromethyl)-4-(3,4,5-trifluorophenyl)-1H-benzimidazol-2-yl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

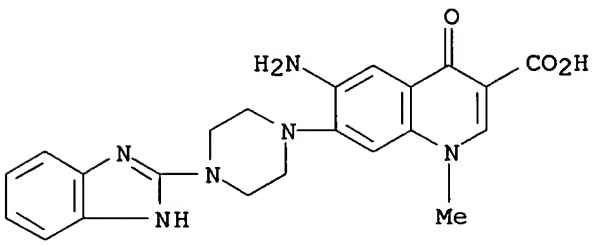
Absolute stereochemistry.



RE.CNT 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:509698 CAPLUS
DN 143:278551
TI Inhibition of cell growth and induction of apoptosis in human prostate cancer cell lines by 6-aminoquinolone WM13

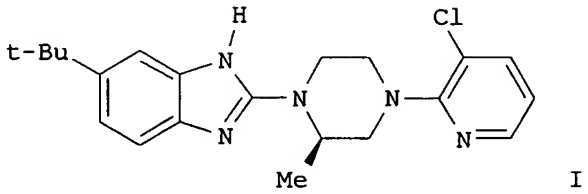
AU Minelli, Alba; Bellezza, Ilaria; Siciliano, Emanuela; Liguori, Lavinia; Tabarrini, Oriana; Cecchetti, Violetta; Fravolini, Arnaldo
CS Dipartimento di Scienze Biochimiche e Biotecnologie Molecolari, Sezione di Biochimica Cellulare, Universita di Perugia, Perugia, 06123, Italy
SO Oncology Reports (2005), 13(6), 1113-1120
CODEN: OCRPEW; ISSN: 1021-335X
PB Oncology Reports
DT Journal
LA English
AB Fluoroquinolones affect the proliferation and apoptotic cell death of several human malignancies. Therefore, we investigated whether new 6-aminoquinolone derivs., initially synthesized as anti-HIV agents, could affect the proliferation and apoptotic cell death of human prostate cancer cell lines. PC3 and LNCaP cell lines were used as models of androgen-resistant and androgen-responsive prostate cancer, and proliferation of PC3 and LNCaP cells was strongly inhibited by 6-aminoquinolone WM13. Cytotoxicity, which was more pronounced in LNCaP, was accompanied by morphol. changes, DNA damage, arrest at the S/G2/M phase of the cell cycle, and an increase of the sub-G1 population. Mol. mechanism underlying WM13-induced cell death involved caspase-8 and -3 and modulation of the expression of apoptotic genes, as well as cleavage of poly-ADP ribose polymerase. Cell death following the treatment of human prostate cancer cell lines with WM13 can be attributed to apoptosis which, depending on the cell line, proceeds through different pathways.
IT **791812-53-8**
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(6-aminoquinolone WM20 exhibited slight inhibition of human prostate cancer cell line PC3, LNCaP proliferation)
RN 791812-53-8 CAPLUS
CN 3-Quinolinecarboxylic acid, 6-amino-7-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-1,4-dihydro-1-methyl-4-oxo- (9CI) (CA INDEX NAME)



RE.CNT 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2005:74690 CAPLUS
DN 142:298063
TI 4-(2-Pyridyl)piperazine-1-benzimidazoles as potent TRPV1 antagonists
AU Shao, Bin; Huang, Jincheng; Sun, Qun; Valenzano, Kenneth J.; Schmid, Lori; Nolan, Scott
CS Purdue Pharma LP, Cranbury, NJ, 08512, USA
SO Bioorganic & Medicinal Chemistry Letters (2005), 15(3), 719-723
CODEN: BMCLE8; ISSN: 0960-894X
PB Elsevier B.V.

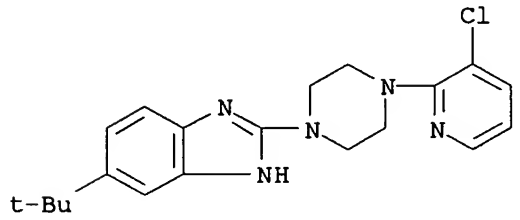
DT Journal
LA English
OS CASREACT 142:298063
GI



I

AB A series of 4-(2-pyridyl)piperazine-1-benzimidazole analogs, e.g., I, was synthesized and evaluated for TRPV1 antagonist activity in capsaicin-induced (CAP) and pH 5.5-induced (pH) FLIPR assays in a human TRPV1-expressing HEK293 cell line. Potent TRPV1 antagonists were identified through SAR studies. From these studies, several antagonists were found, with IC50 values ranging from 32 nM to .apprx.5000 nM. Among these, 11 [IC50 = 90 nM (CAP) and 104 nM (pH)] was further evaluated and found to be orally available in rats (F% = 19.7).

IT **722497-97-4P**
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and TRPV1 affinity and structure-activity relationship of (pyridylpiperazine)benzimidazoles and -benzoxazoles using amination of piperazines with chloropyridines and benzimidazoles or benzoxazole)
RN 722497-97-4 CAPLUS
CN 1H-Benzimidazole, 2-[4-(3-chloro-2-pyridinyl)-1-piperazinyl]-5-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



RE.CNT 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:1124643 CAPLUS
DN 142:93853
TI Drug combinations comprising opioid analgesics and 1-(1,2-disubstituted piperidinyl)-4-substituted piperazines and preparation of the latter.
IN Janssens, Frans Eduard; Sommen, Francois Maria; Leenaerts, Joseph Elisabeth; Van Roosbroeck, Yves Emiel Maria; Meert, Theo Frans
PA Janssen Pharmaceutica N. V., Belg.
SO PCT Int. Appl., 71 pp.
CODEN: PIXXD2

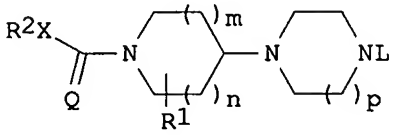
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004110451	A1	20041223	WO 2004-EP51050	20040607

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRAI WO 2003-EP6118 A 20030610
OS MARPAT 142:93853
GI



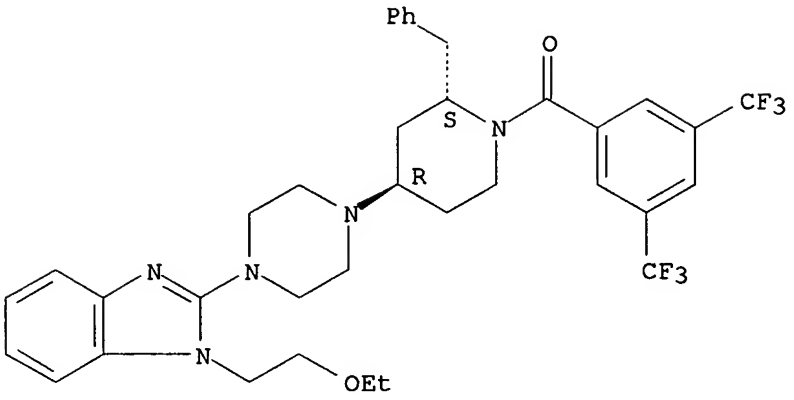
I

AB Claimed is a pharmaceutical compn. comprising a carrier, an opioid analgesic, and a piperazine [I; m, p = 1, 2; n = 0-2; when m = 2, then n = 1; Q = O, NR3; X = bond, O, S, NR3; R1 = (substituted) Ph, phenylalkyl; R2 = naphthyl(alkyl), (substituted) phenyl(alkyl), heterocyclyl(alkyl); R3 = H, alkyl; L = (substituted) Ph, alkyl, alkenyl, aralkenyl, diarylalkenyl, etc.]. Thus, 1-[3,5-bis(trifluoromethyl)benzoyl]-2-benzyl-4-piperidinone (prepn. given) and N-(2,6-dimethylphenyl)-1-piperazineacetamide in CH2Cl2 were treated with Ti(OiPr)4; the mixt. was stirred 3 h followed by addn. of NaBH3CN in EtOH and the mixt. was stirred overnight to give racemic trans- coupling product. This was sepd. on Chiralcel OD using MeOH to obtain (+)-trans-4-[1-[3,5-bis(trifluoromethyl)benzoyl]-2-benzyl-4-piperidinyl]-N-(2,6-dimethylphenyl)-1-piperazineacetamide. The latter as the L-malate salt at 10-40 mg/kg i.p. used with 0.8 mg/kg morphine in ferrets significantly reduced the no. of retches. The pharmaceutical compn. of the invention reduces unwanted side-effects assocd. with opioid analgesics, in particular respiratory depression and tolerance, thereby increasing the total tolerability of said opioids in pain treatment.

IT **190963-35-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(NK1 antagonist; drug combinations comprising opioid analgesics and piperidinylpiperazines)

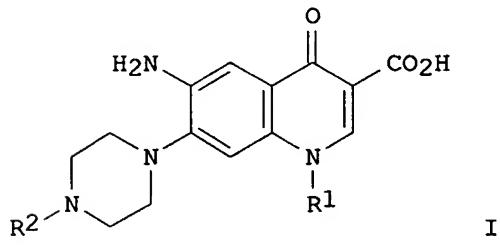
RN 190963-35-0 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:786690 CAPLUS
DN 141:410799
TI Structure Modifications of 6-Aminoquinolones with Potent Anti-HIV Activity
AU Tabarrini, Oriana; Stevens, Miguel; Cecchetti, Violetta; Sabatini, Stefano; Dell'Uomo, Micaela; Manfroni, Giuseppe; Palumbo, Manlio; Pannecouque, Christophe; De Clercq, Erik; Fravolini, Arnaldo
CS Dipartimento di Chimica e Tecnologia del Farmaco, Universita di Perugia, Perugia, 06123, Italy
SO Journal of Medicinal Chemistry (2004), 47(22), 5567-5578
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 141:410799
GI



I

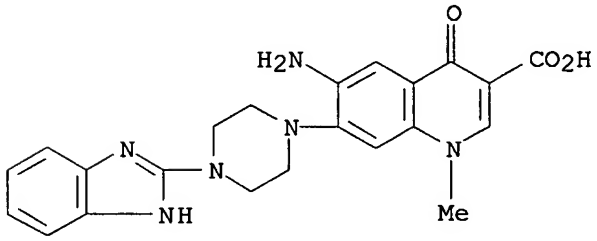
AB It was recently discovered that 6-aminoquinolone derivs. could be valid leads for the development of new anti-HIV agents because of their new and diversified mode of action. The studies carried out on the lead compd. WM5 showed that this deriv. is able to inhibit the Tat-mediated long terminal repeat driven transcription, an essential step in the HIV-1 replication cycle. Thus, starting from lead WM5, the design and synthesis of an enlarged series of 6-aminoquinolones, e.g. I (R1 = Me, 2-benzothiazolyl, biphenyl, 4-FC6H4, etc.; R2 = 2-MeOC6H4, 2-thiazolyl,

2-pyridyl, 5-methyl-1,3,4-thiadiazol-2-yl, etc.), was performed and their structure-activity relationship was studied. I (R1 = Me; R2 = 3-F3CC6H4, 2-thiazolyl, 2-pyrazinyl, 2-benzoxazolyl) proved to be highly effective in inhibiting HIV replication at 50% inhibitory concn. in the range of 0.0087-0.7 .mu.g/mL in MT-4, PBMCs and CEM cell lines coupled with pos. selectivity indexes that reach values higher than 1000 on CEM cell lines for I (R1 = Me; R2 = 2-thiazolyl, 2-pyrazinyl). Time-of-addn. expts. clearly confirm that the new, potent 6-aminoquinolones interact at a postintegration step in the replication cycle of HIV.

IT **791812-53-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of arylpiperazinyl- or heteroarylpiperazinyl-substituted aminoquinolonecarboxylic acids and analogs as anti-HIV agents)

RN 791812-53-8 CAPLUS

CN 3-Quinolinecarboxylic acid, 6-amino-7-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-1,4-dihydro-1-methyl-4-oxo- (9CI) (CA INDEX NAME)



RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

AN 2004:566601 CAPLUS

DN 141:123640

TI Heterocyclylpiperazinylbenzothiazoles, heterocyclylpiperazinylbenzimidazoles, and heterocyclylpiperazinylbenzooxazoles prepared as antagonists for the metabotropic glutamate receptors mGluR1 and mGluR5 and as ligands for human VR1

IN Sun, Qun; Tafesse, Laykea; Victory, Sam

PA Euro-Celtique S.A., Luxembourg

SO PCT Int. Appl., 705 pp.
CODEN: PIXXD2

DT Patent

LA English

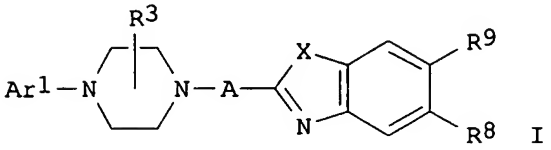
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004058754	A1	20040715	WO 2003-US41100	20031222

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,

ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
US 2004186111 A1 20040923 US 2003-739190 20031219
CA 2511509 AA 20040715 CA 2003-2511509 20031222
EP 1583763 A1 20051012 EP 2003-814351 20031222
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK
BR 2003017757 A 20051122 BR 2003-17757 20031222
NO 2005003582 A 20050907 NO 2005-3582 20050722
PRAI US 2002-435917P P 20021224
US 2003-459626P P 20030403
US 2003-473856P P 20030529
WO 2003-US41100 W 20031222
OS MARPAT 141:123640
GI



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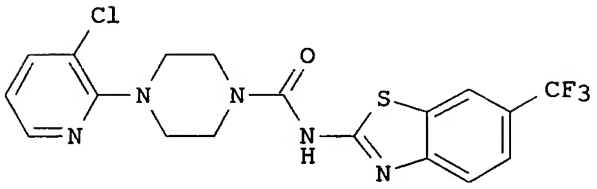
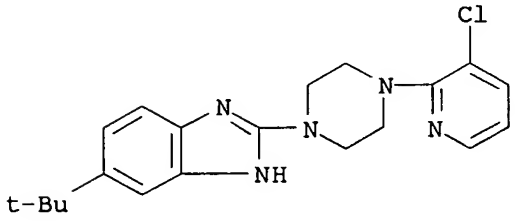


II

AB Heterocyclylpiperazinyl benzothiazoles, benzimidazoles, and benzooxazoles I [A = bond, C(:O)NR4, C(:S)NR4; Ar1 = (un)substituted pyridinyl, pyrazinyl, thiadiazolyl, pyrimidinyl, or pyridazinyl; R3 = H, Me, halogen, cyano, hydroxy, alkoxy, nitro, amino, etc.; X = S, O, NR10; R8, R9 = H, alkyl, alkenyl, alkynyl, cycloalkyl, Ph, halo, halomethyl, dihalomethyl, trihalomethyl, cyano, etc.; R10 = H, alkyl] such as II are prepd. as antagonists for the metabotropic glutamate receptors mGluR1 and mGluR5 and as ligands for the protein VR1 for the treatment of pain, addiction, urinary incontinence, irritable-bowel disorder, inflammatory bowel disease, ulcers, Parkinson's disease, epilepsy, seizures, anxiety, psychosis, stroke, pruritus, cognitive disorders, memory deficits or restricted brain function, Huntington's chorea, amyotrophic lateral sclerosis, retinopathy, muscle spasms, migraines, vomiting, dyskinesia, and depression. Regioselective coupling of 2,3-dichloropyridine and piperazine yields 1-(3-chloro-2-pyridinyl)piperazine (III), while acylation of 6-(trifluoromethyl)-2-aminobenzothiazole with p-nitrophenyl chlorocarbonate yields p-nitrophenyl [6-(trifluoromethyl)-2-benzothiazolyl]carbamate (IV); coupling of III and IV yields II. II gives IC50 values of 262 and 51 (units not indicated) in pH-based and capsaicin-based assays (resp.) for binding to human VR1.

IT **722497-97-4P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)
RN 722497-97-4 CAPLUS
CN 1H-Benzimidazole, 2-[4-(3-chloro-2-pyridinyl)-1-piperazinyl]-5-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)



L4 ANSWER 7 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:354920 CAPLUS
DN 140:375171
TI Preparation of benzimidazoles as vanilloid receptor ligands
IN Balan, Chenera; Bo, Yunxin; Dominguez, Celia; Fotsch, Christopher H.; Gore, Vijay K.; Ma, Vu Van; Norman, Mark H.; Ognyanov, Vassil I.; Qian, Yi-xin; Wang, Xianghong; Xi, Ning; Xu, Shimin
PA Amgen Inc., USA
SO PCT Int. Appl., 259 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004035549	A1	20040429	WO 2003-US32823	20031016
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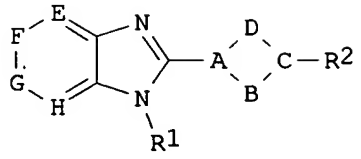
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2501539	AA	20040429	CA 2003-2501539	20031016
	US 2004152690	A1	20040805	US 2003-688246	20031016
	EP 1551811	A1	20050713	EP 2003-809075	20031016
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
PRAI	US 2002-419791P	P	20021017		
	WO 2003-US32823	W	20031016		

OS MARPAT 140:375171

GI



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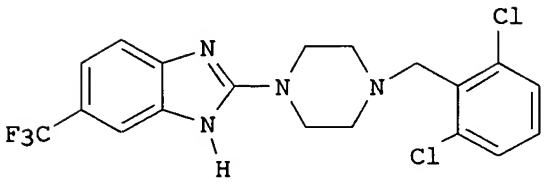


II

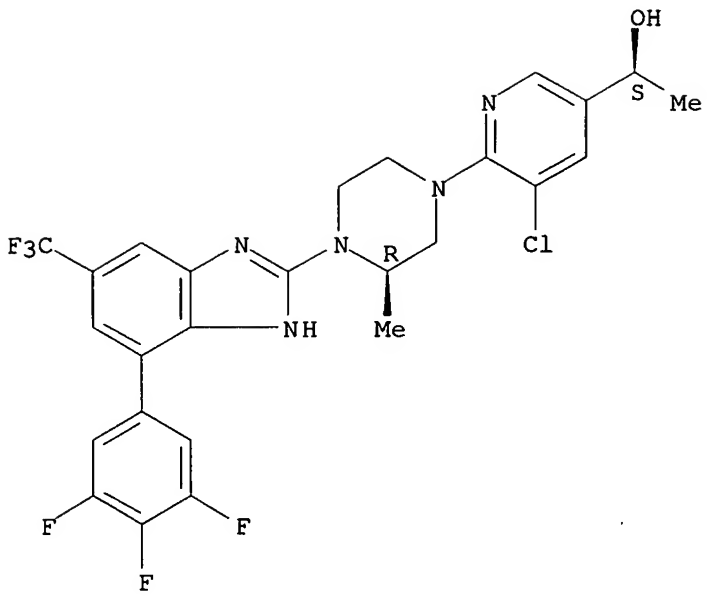
AB Title compds. I [wherein B, D = independently substituted un/partially/satd. C1-C3 chain, with provisos; A, C = independently N, CH and derivs. with at least one of A and C is N; E, F, G, H = independently N, CH and derivs.; R1 = H, (CH2)mR3 and derivs.; m = 0,1 or 2; R3 = independently (un)substituted un/partially/satd. 5, 6, or 7-membered monocyclic, or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring contg. 0-4 heteroatoms selected from N, O, and S] were prepd. as vanilloid receptor ligands (no data). For example, II was prepd. by alkylation of piperazine with 2-chloro-6-trifluoromethyl-1H-benzimidazole(prepn. given) in DMSO and reaction with 2,6-dichlorobenzyl bromide in DMF. Tests for capsaicin agonist and antagonist properties at vanilloid receptor type 1 are given (no data). I are useful in the treatment of vanilloid-receptor-mediated diseases, such as inflammatory or neuropathic pain and diseases involving sensory nerve function such as asthma, rheumatoid arthritis, osteoarthritis, inflammatory bowel disorders, urinary incontinence, migraine and psoriasis (no data).

IT **683244-16-8P**, (1S)-1-[5-Chloro-6-[(3R)-3-methyl-4-[5-trifluoromethyl-7-(3,4,5-trifluorophenyl)-1H-benzimidazol-2-yl]piperazin-1-yl]pyridin-3-yl]ethanol
RL: PAC (Pharmacological activity); PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of benzimidazoles as vanilloid receptor ligands)

RN 683244-16-8 CAPLUS

CN 3-Pyridinemethanol, 5-chloro-.alpha.-methyl-6-[(3R)-3-methyl-4-[6-(trifluoromethyl)-4-(3,4,5-trifluorophenyl)-1H-benzimidazol-2-yl]-1-piperazinyl]-, (.alpha.S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:20661 CAPLUS
DN 140:93938
TI Preparation of substituted quinolines useful as CCR5 receptor antagonists
IN Dunning, Laura; Jaroch, Stefan; Kochanny, Monica J.; Lee, Wheeseong; Lian, Xiongdong; Liang, Meina; Lu, Shou-Fu; Onuffer, James; Phillips, Gary; Wei, Guo-Ping; Ye, Bin
PA Schering Aktiengesellschaft, Germany
SO PCT Int. Appl., 241 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004002960	A1	20040108	WO 2003-US20950	20030624
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2489560	AA	20040108	CA 2003-2489560	20030624
	BR 2003012204	A	20050426	BR 2003-12204	20030624
	EP 1534681	A1	20050601	EP 2003-762325	20030624
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

	JP 2005537247	T2	20051208	JP 2004-518228	20030624
	US 2004072818	A1	20040415	US 2003-607530	20030626
	NO 2005000429	A	20050329	NO 2005-429	20050126
PRAI	US 2002-451687P	P	20020627		
	WO 2003-US20950	W	20030624		

OS MARPAT 140:93938
GI

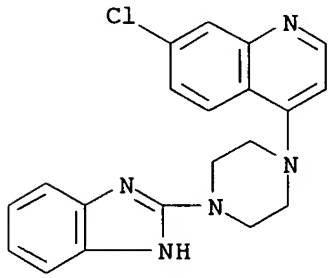
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to quinoline derivs. of formula I and II [wherein: R1, R1* = H, (un)substituted amino, alkyl, haloalkyl, OH, alkoxy, CO2R9a; R2, R2*, R3, R3* = H, (halo)alkyl, halogen, (un)substituted amino, nitro, cyano, alkoxy; R4, R4* = H, alkyl; R5 = H, R9, R9-aminocycloalk(en)yl, (alk/aryl)oxycarbonyl, SO2R9, C(O)NR7R9, C(O)NR7-SO2R9, C(O)R6, C(O)R9, C(=NR10)R9, C(S)R9, C(=NR10)NHR9, C(S)NHR9, C(S)NR7-SO2R9; R6 is a group of formula III; R7, R7* = H, (un)substituted alkyl or aryl; R9a = arylalkyl, cycloalk(en)yl, cycloalkylalkyl, alkyl, heterocyclylalkyl, aryl, heterocyclyl any of which can be (un)substituted; R9 is same as R9a except H; R10 = H, cyano, (un)substituted alkyl or alkoxy; n = 0-3, n* = 1-3], their enantiomers, diastereomers, salts, and solvates. For instance, quinoline IV was prepd. via amination of 4,7-dichloroquinoline by piperazine, and subsequent addn. of obtained 7-chloro-4-(piperazin-1-yl)quinoline to 4-FC6H4NCO. The invention compds. are claimed as CCR5 receptor antagonists (no data) and useful for treating the CCR5-mediated inflammatory and immunoregulatory disorders such as optic neuritis, stroke, dermatitis, HIV, diabetes, etc.

IT **643042-39-1P**, 4-[4-(Benzimidazol-2-yl)piperazin-1-yl]-7-chloroquinoline
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinoline derivs. useful as CCR5 receptor antagonists)

RN 643042-39-1 CAPLUS

CN Quinoline, 4-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-7-chloro- (9CI) (CA INDEX NAME)



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:539807 CAPLUS

DN 139:69267
TI Preparation of 2-benzimidazolylamines as ORL1-receptor agonists for the treatment of pain and inflammatory diseases
IN Ito, Fumitaka
PA Pfizer Inc., USA
SO Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1069124	A1	20010117	EP 2000-305981	20000714
	EP 1069124	B1	20040512		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6340681	B1	20020122	US 2000-606921	20000629
	JP 2001048879	A2	20010220	JP 2000-209374	20000711
	JP 3276111	B2	20020422		
	JP 2001039974	A2	20010213	JP 2000-211264	20000712
	BR 2000002796	A	20010403	BR 2000-2796	20000714
	AT 266657	E	20040515	AT 2000-305981	20000714
	PT 1069124	T	20040930	PT 2000-305981	20000714
	ES 2219272	T3	20041201	ES 2000-305981	20000714
	CA 2314008	AA	20010116	CA 2000-2314008	20000717
PRAI	WO 1999-IB1290	W	19990716		

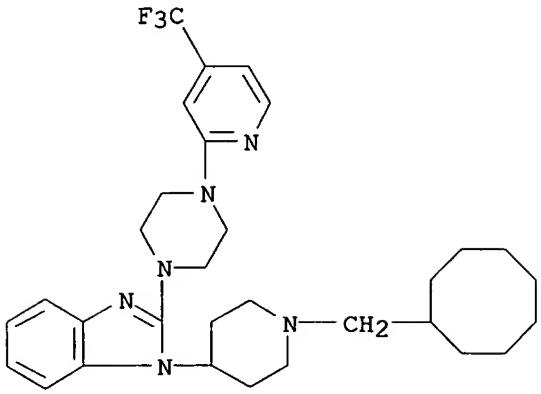
OS MARPAT 139:69267
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1, R2 = H, halo, OH, etc.; R3, R4 = H, halo-alkyl, substituted alkyl, i.e., OH, alkoxy, alkyl-S, etc.; R5 = pheny, substituted cycloalkyl, i.e., H, halo, OH, etc.;] and their pharmaceutically acceptable salts were prepd. For example, N-alkylation of N-methylpiperazine by chlorobenzimidazolyl II, e.g., prepd. from 1,3-dihydro-1-(4-piperidinyl)-2H-benzimidazol-2-one in 2-steps, afforded 2-benzimidazolylamine III in 15% yield. In selective affinity studies of opioid receptors, i.e., ORL1, .mu., .kappa. and .delta., some examples of compds. I exhibited good ORL1-receptor agonist activity. Compds. I are claimed useful as analgesics.

IT **548794-06-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(target compd.; prepn. of 2-benzimidazolylamines as ORL1-receptor agonists for the treatment of pain and inflammatory diseases)

RN 548794-06-5 CAPLUS
CN 1H-Benzimidazole, 1-[1-(cyclooctylmethyl)-4-piperidinyl]-2-[4-[4-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

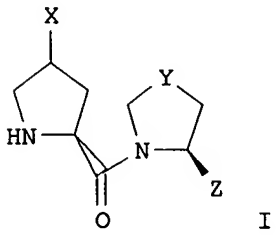


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:142666 CAPLUS
DN 136:200479
TI Preparation of proline derivatives as dipeptidyl peptidase IV (DPP-IV) inhibitors and use thereof as drugs
IN Kitajima, Hiroshi; Sakashita, Hiroshi; Akahoshi, Fumihiko; Hayashi, Yoshiharu
PA Welfide Corporation, Japan
SO PCT Int. Appl., 340 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002014271	A1	20020221	WO 2001-JP6906	20010810
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2418656	AA	20020221	CA 2001-2418656	20010810
	AU 2001077754	A5	20020225	AU 2001-77754	20010810
	EP 1308439	A1	20030507	EP 2001-955660	20010810
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001013146	A	20030624	BR 2001-13146	20010810
	NZ 524618	A	20040827	NZ 2001-524618	20010810
	NO 2003000619	A	20030226	NO 2003-619	20030207
	US 2004106655	A1	20040603	US 2003-344255	20030210
	US 2005245538	A1	20051103	US 2005-142523	20050602
PRAI	JP 2000-243217	A	20000810		
	JP 2000-400296	A	20001228		
	WO 2001-JP6906	W	20010810		

US 2003-344255 A3 20030210
OS MARPAT 136:200479
GI



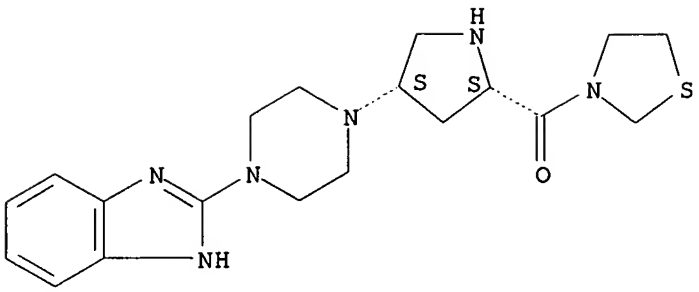
I

AB The title compds. [I; X = NR1R2, NR3COR4, NR5COR4, NR5CH2CH2NR6R7, NR8SO2R9, OR10, O2CR11; wherein R1, R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, or they are linked to each other to form a heterocyclyl contg. 1 or 2 N atoms or O which may be a spiro ring and is optionally fused to an (un)substituted arom. ring; R3, R4 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, arylalkenyl, heteroaryl, heteroarylalkyl; R5, R6, R7 = H, alkyl, acyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl, or which is optionally fused to an (un)substituted arom. ring; R8, R9, R10, R11 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl] or pharmacol. acceptable salts thereof are prepd. These compds. are useful for the treatment of DPP-IV related diseases such as diabetes, obesity, HIV infection, cancer metastasis, skin diseases, prostatic hypertrophy (prostatomegaly), pericementitis, or autoimmune diseases. Thus, a soln. of 0.924 g (S)-1-[(2S,4S)-4-amino-1-tert-butoxycarbonyl-2-pyrrolidinylcarbonyl]-2-cyanopyrrolidine (prepn. given), 1.7 mL diisopropylethylamine, and 0.78 g 2-chloro-4-fluorobenzonitrile in 10 mL N-methyl-2-pyrrolidone were stirred at 80.degree. for 4 h to give 0.94 g (S)-1-[(2S,4S)-1-tert-butoxycarbonyl-4-(3-chloro-4-cyanophenyl)amino-2-pyrrolidinylcarbonyl]-2-cyanopyrrolidine which (0.93 g) was treated with HCl/EtOAc at room temp. for 15 h to give (S)-1-[(2S,4S)-4-(3-chloro-4-cyanophenyl)amino-2-pyrrolidinylcarbonyl]-2-cyanopyrrolidine hydrochloride (II). II showed IC50 of 0.13 and 0.15 nM against human blood plasma DPP-IV and rat blood plasma DPP-IV, resp.

IT **401563-25-5P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline derivs. as dipeptidyl peptidase IV (DPP-IV) inhibitors for treating DPP-IV related diseases)

RN 401563-25-5 CAPLUS
CN Thiazolidine, 3-[[(2S,4S)-4-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, dihydrochloride (9CI) (CA INDEX NAME)

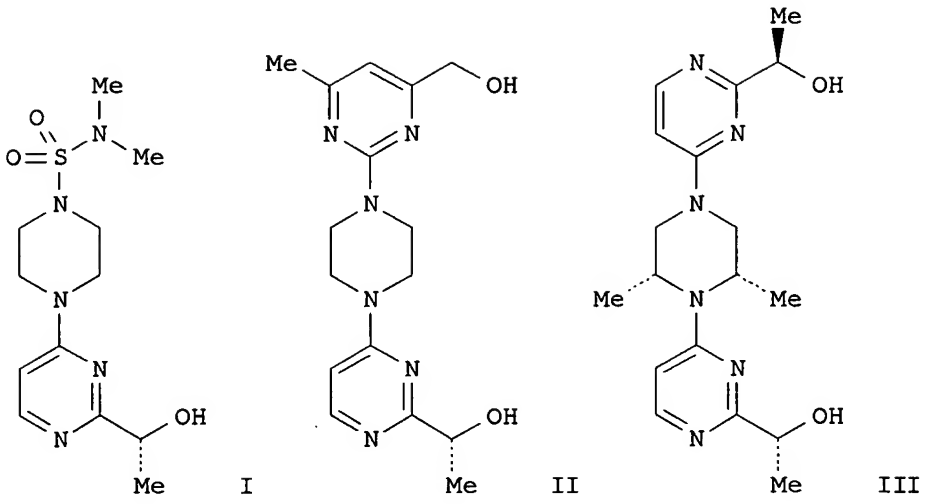
Absolute stereochemistry.



●2 HCl

RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:916027 CAPLUS
DN 136:200160
TI Orally-Effective, Long-Acting Sorbitol Dehydrogenase Inhibitors: Synthesis, Structure-Activity Relationships, and in Vivo Evaluations of Novel Heterocycle-Substituted Piperazino-Pyrimidines
AU Chu-Moyer, Margaret Y.; Ballinger, William E.; Beebe, David A.; Berger, Richard; Coutcher, James B.; Day, Wesley W.; Li, Jiancheng; Mylari, Banavara L.; Oates, Peter J.; Weekly, R. Matthew
CS Departments of Cardiovascular and Metabolic Disease and Drug Metabolism Development, Pfizer Global Research and Development, Groton Laboratories, Groton, CT, 06340, USA
SO Journal of Medicinal Chemistry (2002), 45(2), 511-528
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English
OS CASREACT 136:200160
GI



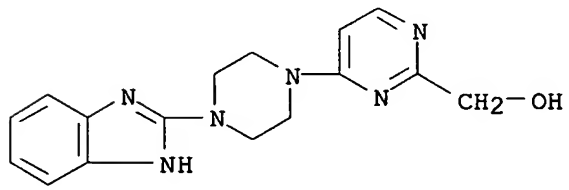
I II III

AB Optimization of a previously disclosed sorbitol dehydrogenase inhibitor (SDI, I) for potency and duration of action was achieved by replacing the metabolically labile N,N-dimethylsulfamoyl group with a variety of heterocycles. Specifically, this effort led to a series of novel, in vitro potent SDI's, e.g. the [[(hydroxymethylpyrimidinyl)piperazinyl]pyrim idinyl]ethanol II, with longer serum half-lives and acceptable in vivo activity in acutely diabetic rats. However, the desired in vivo potency in chronically diabetic rats, ED90 .ltoreq. 5 mg/kg/day, was achieved only through further modification of the piperazine linker. Several members of this family, including [[(hydroxyethylpyrimidinyl)dimethylpiperazinyl]pyri midinyl]ethanol III, showed better than the targeted potency with ED90 values of 1-2 mg/kg/day. III was further profiled and found to be a selective inhibitor of sorbitol dehydrogenase, with excellent pharmacodynamic/pharmacokinetic properties, demonstrating normalization of sciatic nerve fructose in a chronically diabetic rat model for .apprx.17 h, when administered orally at a single dose of 2 mg/kg/day.

IT **400785-12-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and structure-activity relationships of oral antidiabetic, sorbitol dehydrogenase-inhibiting heterocyclic piperazinopyrimidines)

RN 400785-12-8 CAPLUS

CN 2-Pyrimidinemethanol, 4-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

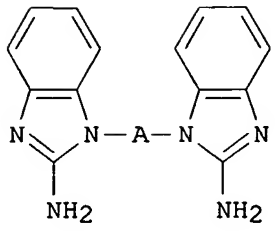


RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:34861 CAPLUS
DN 132:93320
TI Preparation of aminobenzimidazoles and guanidines as novel potassium channel blocking agents
IN Teuber, Lene; Olesen, Soren-Peter; Strobaek, Dorte; Jensen, Bo Skaaning; Peters, Dan
PA Neurosearch A/S, Den.
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000001676	A1	20000113	WO 1999-DK378	19990701
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9947689	A1	20000124	AU 1999-47689	19990701
	EP 1091942	A1	20010418	EP 1999-931019	19990701
	EP 1091942	B1	20050330		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002519412	T2	20020702	JP 2000-558081	19990701
	AT 292120	E	20050415	AT 1999-931019	19990701
	US 6194447	B1	20010227	US 1999-347514	19990702
	US 2002049246	A1	20020425	US 2000-750345	20001229
	US 6380180	B2	20020430		
	US 2002137784	A1	20020926	US 2002-84179	20020228
	US 6569880	B2	20030527		
PRAI	DK 1998-865	A	19980702		
	US 1998-92218P	P	19980708		
	WO 1999-DK378	W	19990701		
	US 1999-347514	A3	19990702		
	US 2000-750345	A3	20001229		

OS MARPAT 132:93320
GI



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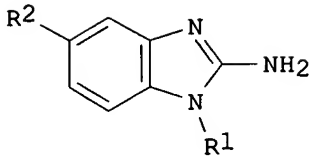
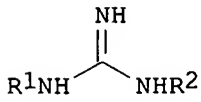


II



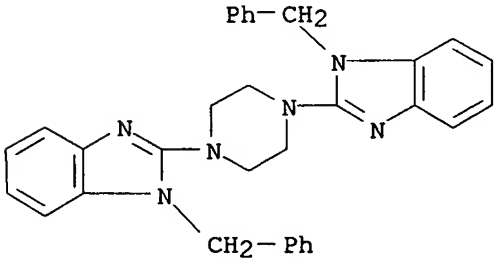
III

AB The title compds. [I (A = a spacing group contg. of 1-20 atoms), II (R1 = mono- or polycyclic (un)substituted aryl, aralkyl, mono- or polycyclic heterocyclyl, etc.; R2 = H, alkyl, CF3), III (R1, R2 = H, alkyl, mono- or polycyclic heterocyclyl, etc.), etc.], useful for the treatment or alleviation of diseases or disorders assocd. with the activity of potassium channels, in particular asthma, cystic fibrosis, chronic obstructive pulmonary disease, convulsions, vascular spasms, coronary artery spasms, renal disorders, etc., were prepd. Thus, treatment of N,N'-bis(2-aminophenyl)-1,4-butanediamine.2HCl (prepn. given) with cyanogen bromide in DMF afforded I [A = (CH)4]. Biol. data for some of the title compds. were given.

IT **254434-82-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminobenzimidazoles and guanidines as potassium channel blocking agents)

RN 254434-82-7 CAPLUS

CN 1H-Benzimidazole, 2,2'-(1,4-piperazinediyl)bis[1-(phenylmethyl)- (9CI) (CA INDEX NAME)



RE.CNT 104 THERE ARE 104 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1997:425258 CAPLUS
DN 127:34245
TI Preparation of 1-(1,2-disubstituted piperidinyl)-4-substituted piperazine derivatives as substance-P antagonists
IN Janssens, Frans Eduard; Sommen, Francois Maria; Surleraux, Dominique Louis Nestor Ghislaine; Leenaerts, Joseph Elisabeth; Van Roosbroeck, Yves Emiel Maria
PA Janssen Pharmaceutica N.V., Belg.; Janssens, Frans Eduard; Sommen, Francois Maria; Surleraux, Dominique Louis Nestor Ghislaine; Leenaerts, Joseph Elisabeth; Van Roosbroeck, Yves Emiel Maria
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9716440	A1	19970509	WO 1996-EP4660	19961025
	W: AL, AM, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
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	TW 460473	B	20011021	TW 1996-85113017	19961024
	CA 2234096	AA	19970509	CA 1996-2234096	19961025
	CA 2234096	C	19970509		
	AU 9674932	A1	19970522	AU 1996-74932	19961025
	AU 704155	B2	19990415		
	EP 862566	A1	19980909	EP 1996-937248	19961025
	EP 862566	B1	20000112		
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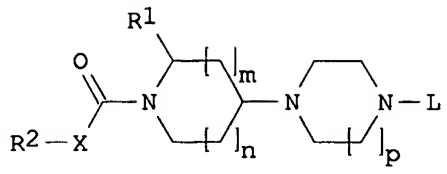
	CN 1205699	A	19990120	CN 1996-199225	19961025
	CN 1117744	B	20030813		
	BR 9611184	A	19990330	BR 1996-11184	19961025
	JP 11514634	T2	19991214	JP 1997-517050	19961025
	JP 3073238	B2	20000807		
	AT 188691	E	20000115	AT 1996-937248	19961025
	ES 2143238	T3	20000501	ES 1996-937248	19961025
	PT 862566	T	20000630	PT 1996-937248	19961025
	IL 123962	A1	20010111	IL 1996-123962	19961025
	PL 185029	B1	20030228	PL 1996-327406	19961025
	CZ 291794	B6	20030514	CZ 1998-1322	19961025
	ZA 9609090	A	19980429	ZA 1996-9090	19961029
	HR 960507	B1	20010831	HR 1996-960507	19961030
	NO 9801534	A	19980624	NO 1998-1534	19980403
	NO 310232	B1	20010611		
	US 6197772	B1	20010306	US 1998-54963	19980403
	GR 3033154	T3	20000831	GR 2000-400847	20000404
	US 6521621	B1	20030218	US 2000-745513	20001222
	US 37886	E	20021015	US 2001-935698	20010823
	CN 1438220	A	20030827	CN 2002-157427	20021217
PRAI	EP 1995-202929	A	19951030		
	EP 1996-937248	A	19961025		
	WO 1996-EP4660	W	19961025		
	US 1998-54963	A1	19980403		

OS MARPAT 127:34245
GI



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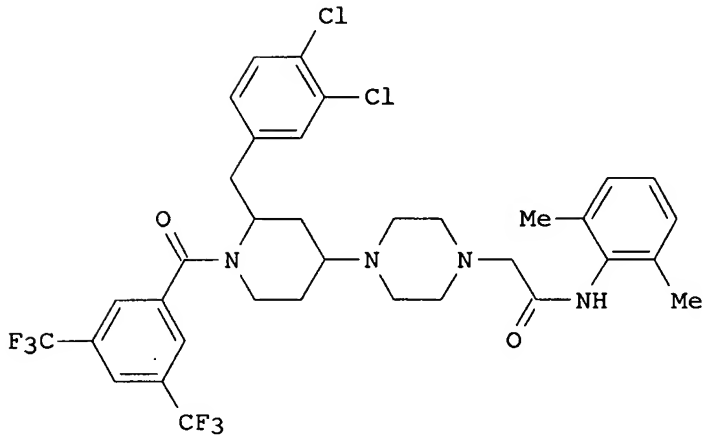


II

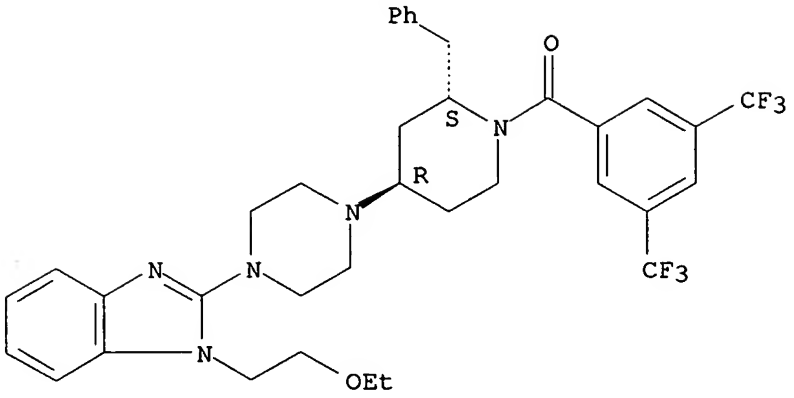
AB The title compds. [I; n = 0-2; m = 1-2 (if m = 2, then n = 1); p = 1-2; Q = O, NR3; X = a covalent bond, a bivalent radical of formula O, S, NR3; R1 = Ar1, Ar1C1-6alkyl, di(Ar1)C1-6alkyl (wherein each C1-6alkyl group is optionally substituted with hydroxy, C1-4alkyloxy, oxo, a ketalized oxo substituent); R2 = Ar2, Ar2C1-6alkyl, Het1, Het1C1-6alkyl; R3 = H, C1-6alkyl; L = H; Ar3; C1-6alkyl, etc.Ar1, Ar2, Ar3 = (un)substituted Ph; Het1, Het2 = monocyclic, bicyclic heterocycle] and their N-oxide forms, the pharmaceutically acceptable addn. salts and the stereoisomeric forms, useful as substance-P antagonists were prepd. and formulated. Thus, reaction of 3,5-bis(trifluoromethyl)benzoyl chloride with (.+-.)-trans-4-[2-[(3,4-dichlorophenyl)methyl]-4-piperidinyl}-N-(2,6-dimethylphenyl)-1-piperazineacetamide in the presence of Et3N in DCM afforded 44% II which showed IC50 of 0.13x10-9 M against substance-P induced relaxation of the pig coronary arteries.

IT **190963-35-0P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-(1,2-disubstituted piperidinyl)-4-substituted piperazine derivs. as substance-P antagonists)

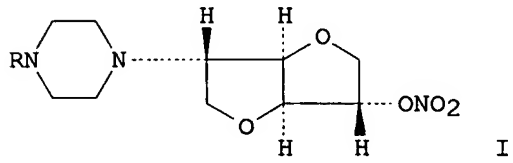
RN 190963-35-0 CAPLUS

CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:218319 CAPLUS
DN 120:218319
TI 1,4:3,6-Dianhydrohexitol nitrate derivatives. II. Synthesis and antianginal activity of aryl- or arylcarbonylpiperazine derivatives
AU Hayashi, Hiroaki; Ikeda, Junichi; Kubo, Kazuhiro; Moriyama, Takahiro; Karasawa, Akira; Suzuki, Fumio
CS Pharm. Res. Lab., Kyotwa Hakko Dogyo Co., Ltd., Nagaizumi, 411, Japan
SO Chemical & Pharmaceutical Bulletin (1993), 41(6), 1100-10
CODEN: CPBTAL; ISSN: 0009-2363
DT Journal
LA English
GI

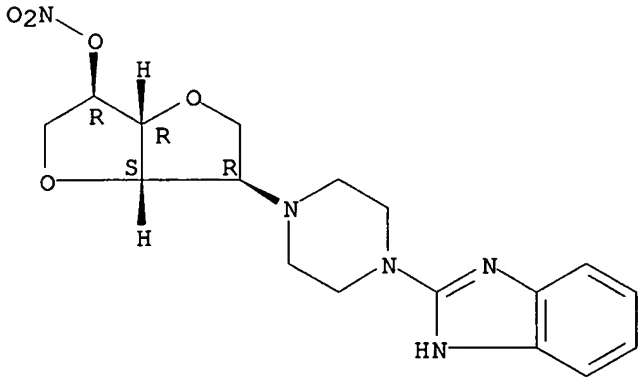


I

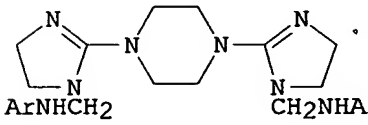
AB A series of 5-(4-aryl- or 4-arylcarbonylpiperazin-1-yl)-5-deoxy-1,4:3,6-dianhydro-L-iditol 2-nitrates, I (R = aryl, arylcarbonyl), was prepd. in order to obtain orally active, nitrate-type vasodilators with reduced side effects. The drug design was based on a small redn. in the lipophilicity compared to that of I (R = H) (KF14124). Compds. I [R = benzimidazol-2-yl, nicotinoyl (KW-3196), 3-furoyl] showed potent anti-ischemic activity in a lysine-vasopressin-induced angina pectoris model (rats); their structure-activity relationships are discussed. Compd. KW-3196 exhibited potent vasodilation of the coronary artery in anesthetized dogs and also exhibited potent preload redn. in a heart failure model (dogs) as compared with isosorbide dinitrate, nicorandil, and KF14124. Furthermore, KW-3196 showed much weaker acute lethal toxicity and less central nervous system depression than KF14124 in mice. Thus, KW-3196 is under development as a vasodilator and a drug for treating angina pectoris.

IT **153843-31-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antianginal activity)
RN 153843-31-3 CAPLUS
CN D-Iditol, 1,4:3,6-dianhydro-2-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-2-deoxy-, 5-nitrate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1992:83632 CAPLUS
DN 116:83632
TI Synthesis and antiparkinsonian activity of 2,2'-(1,4-piperazinediyl)bis[N-(substituted phenyl)-4,5-dihydro-1H-imidazole-1-methanamines] and 2,2'-(1,4-piperazinediyl)bis[N-(substituted phenyl)-1H-benzimidazole-1-methanamines]
AU Naithani, Pankaj K.; Bhalla, Manish; Palit, Gautam; Srivastava, V. K.; Shankar, K.
CS Dep. Pharmacol. Ther., King George's Med. Coll., Lucknow, 226 003, India
SO Indian Journal of Heterocyclic Chemistry (1991), 1(2), 65-70
CODEN: IJCHEI; ISSN: 0971-1627
DT Journal
LA English
GI



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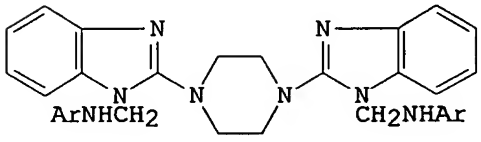


II

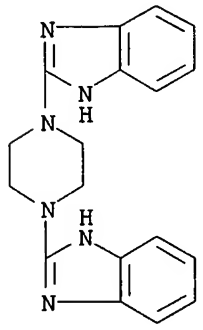
AB Piperazines I (Ar = Ph, 2-MeC6H4, 4-ClC6H4, 4-MeOC6H4, 2,5-Cl2C6H3) and II were synthesized in 3 steps from 1,4-dicyanopiperazine and screened for their antiparkinsonian activity and toxicity. I (Ar = 4-ClC6H4), the most

active compd., when screened for its dopamine (DA) receptor binding activity, showed affinity for DA receptors.

IT **138768-65-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and Mannich reactions of)

RN 138768-65-7 CAPLUS

CN 1H-Benzimidazole, 2,2'-(1,4-piperazinediyl)bis- (9CI) (CA INDEX NAME)



L4 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1991:536644 CAPLUS

DN 115:136644

TI Preparation of heterocyclylhexitols as coronary vasodilators

IN Suzuki, Fumio; Hayashi, Hiroaki; Kuroda, Takeshi; Kubo, Kazuhiro; Ikeda, Junichi

PA Kyowa Hakko Kogyo Co., Ltd., Japan

SO Eur. Pat. Appl., 92 pp.
CODEN: EPXXDW

DT Patent

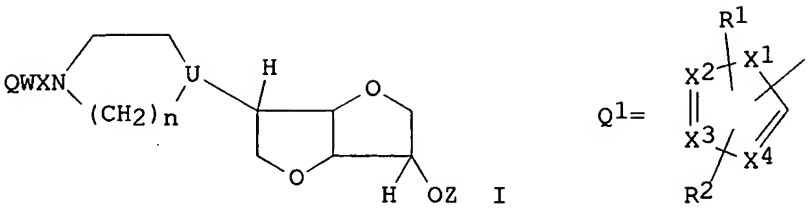
LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 393574	A2	19901024	EP 1990-107245	19900417
	EP 393574	A3	19910821		
	EP 393574	B1	19960131		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE				
	CA 2014520	AA	19901017	CA 1990-2014520	19900412
	CA 2014520	C	19960716		
	US 5053408	A	19911001	US 1990-508701	19900413
	JP 03218381	A2	19910925	JP 1990-100005	19900416
	JP 2954647	B2	19990927		
	AT 133671	E	19960215	AT 1990-107245	19900417
	ES 2085295	T3	19960601	ES 1990-107245	19900417
PRAI	JP 1989-97032	A	19890417		
	JP 1989-293125	A	19891110		

OS MARPAT 115:136644

GI



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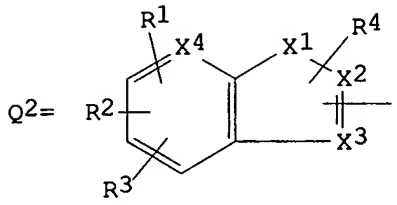
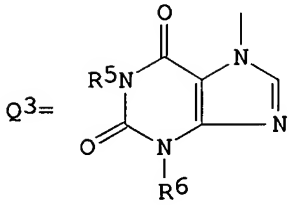
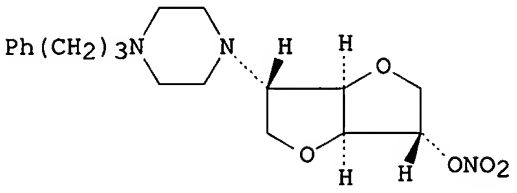






II

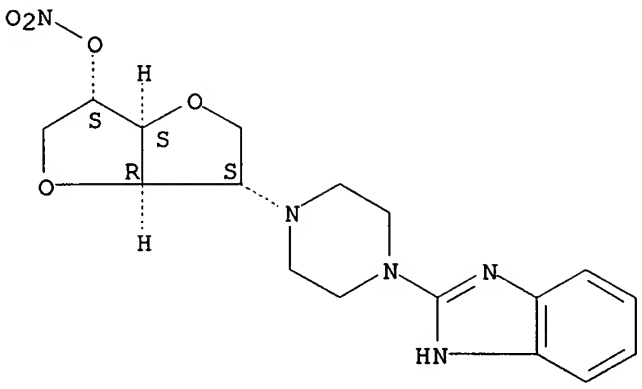
AB Title compds. [I; Q = Q1, Q2, Q3, etc.; X1 = NH, O, S; X2-X4 = CH, N; R1-R4 = H, alkyl, CF3, aryl, alkanoyloxy, amino, alkanoyl, halo, NO2, etc.; R5, R6 = H, alkyl; U = N, N(O); W = bond, O, S; X = (CY1Y2)l, CY3:CY4 = (CY1Y2)l; Y1, Y2 = H, alkyl, OH, alkanoyloxy, cyano, Ph; Y1Y2 = O; Y3, Y4 = H, alkyl; l = 0-6; Z = H, NO2; n = 2, 3], were prepd. Thus, a mixt. of 1,4:3,6-dianhydro-D-glucitol 5-methanesulfonate was refluxed 36 h with piperazine in BuOH to give 5-deoxy-5-piperazin-1-yl-1,4:3,6-dianhydro-L-iditol methanesulfonate. The latter in aq. H2SO4 was added to a -15.degree. mixt. of urea and 86% HNO3 in conc. H2SO4 to give 38% 5-deoxy-5-piperazin-1-yl-1,4:3,6-dianhydro-L-iditol 2-nitrate. The latter was refluxed 24 h with 1-chloro-3-phenylthiopropane and Et3N in EtOH to give 34% of title compd. II. II at 0.3 mg/kg i.d. was effective against propranolol-induced heart failure in dogs.

IT **134186-00-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as coronary vasodilator)

RN 134186-00-8 CAPLUS

CN L-Iditol, 1,4:3,6-dianhydro-2-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-2-deoxy-, 5-nitrate, hydrochloride (9CI) (CA INDEX NAME)

Absolute stereochemistry.



●x HCl

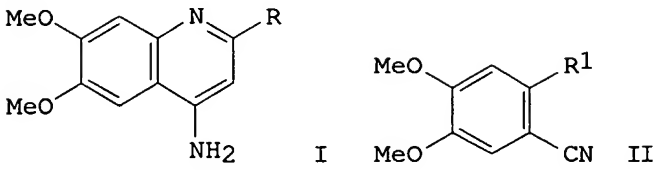
L4 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1984:407051 CAPLUS
DN 101:7051
TI 2-Substituted 4-amino-6,7-dimethoxyquinolines
IN Campbell, Simon Fraser; Hardstone, John David
PA Pfizer Ltd., UK; Pfizer Corp.
SO Eur. Pat. Appl., 51 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 100200	A1	19840208	EP 1983-304196	19830720
	EP 100200	B1	19870506		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	US 4656174	A	19870407	US 1983-515095	19830719
	AT 26978	E	19870515	AT 1983-304196	19830720
	FI 8302658	A	19840125	FI 1983-2658	19830721
	FI 78296	B	19890331		
	FI 78296	C	19890710		
	ES 524320	A1	19850416	ES 1983-524320	19830721
	PL 139498	B1	19870131	PL 1983-243131	19830721
	DK 8303373	A	19840125	DK 1983-3373	19830722
	DK 166821	B1	19930719		
	NO 8302688	A	19840125	NO 1983-2688	19830722
	NO 171594	B	19921228		
	NO 171594	C	19930407		
	AU 8317222	A1	19840126	AU 1983-17222	19830722
	AU 548036	B2	19851121		
	JP 59033264	A2	19840223	JP 1983-134244	19830722
	JP 02019112	B4	19900427		
	HU 31688	O	19840528	HU 1983-2594	19830722
	HU 190907	B	19861228		
	ZA 8305355	A	19840530	ZA 1983-5355	19830722
	DD 211555	A5	19840718	DD 1983-253330	19830722

	SU 1251801	A3	19860815	SU 1983-3618703	19830722
	CS 247073	B2	19861113	CS 1983-5509	19830722
	IL 69311	A1	19870130	IL 1983-69311	19830722
	CA 1255670	A1	19890613	CA 1983-433023	19830722
	SU 1340589	A3	19870923	SU 1984-3732816	19840426
	US 4686228	A	19870811	US 1986-925029	19861030
	US 4758568	A	19880719	US 1987-48343	19870511
	NO 9003181	A	19840125	NO 1990-3181	19900717
	NO 173605	B	19930927		
	NO 173605	C	19940105		
PRAI	GB 1982-21457	A	19820724		
	US 1983-515095	A3	19830719		
	EP 1983-304196	A	19830720		
	NO 1983-2688	A1	19830722		
	US 1986-925029	A3	19861030		

OS MARPAT 101:7051

GI

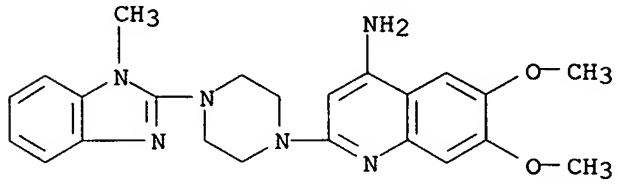


AB Antihypertensive (no data) aminodimethoxyquinolines I (R = tertiary amino) were prepd. Thus the aniline II (R1 = NH2) was treated with MeC(OEt)3 to give II (R1 = N:CMeOEt) which was treated with N-benzylpiperazine to give II [R1 = 1-(4-benzylpiperazino)ethylideneamino, III]. Cyclization of III with ZnCl2 gave I (R = 4-benzylpiperazino) which was hydrogenolyzed to I (R = piperazino). Acylation of I (R = piperazino) with 1,4-benzodioxan-2-carbonyl chloride gave I [R = 4-(1,4-benzodioxan-2-ylcarbonyl)piperazino].

IT **90402-23-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 90402-23-6 CAPLUS

CN 4-Quinolinamine, 6,7-dimethoxy-2-[4-(1-methyl-1H-benzimidazol-2-yl)-1-piperazinyl]-, dihydrochloride (9CI) (CA INDEX NAME)

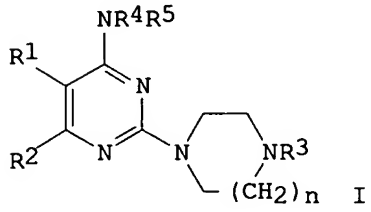


●2 HCl

L4 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1983:34596 CAPLUS
DN 98:34596
TI 2-(Piperazinyl)-4-pyrimidinamines
IN Rakhit, Sumanas; Bagli, Jehan F.
PA American Home Products Corp., USA
SO U.S., 14 pp. Cont.-in-part of U.S. 4,333,937.
CODEN: USXXAM
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4351832	A	19820928	US 1981-245798	19810320
	US 4333937	A	19820608	US 1980-141548	19800418
	ZA 8102354	A	19821124	ZA 1981-2354	19810408
	CA 1152986	A1	19830830	CA 1981-375300	19810413
	WO 8103022	A1	19811029	WO 1981-US502	19810416
	W: AU, DK, HU, JP, SU				
	RW: AT, CH, DE, FR, GB, LU, NL, SE				
	EP 39190	A1	19811104	EP 1981-301719	19810416
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8170789	A1	19811110	AU 1981-70789	19810416
	JP 57500561	T2	19820401	JP 1981-501442	19810416
	EP 56027	A1	19820721	EP 1981-901112	19810416
	R: AT, CH, DE, FR, GB, LU, NL, SE				
	DK 8105624	A	19811217	DK 1981-5624	19811217
PRAI	US 1980-141548	A2	19800418		
	US 1981-245798	A	19810320		
	WO 1981-US502	A	19810416		

OS CASREACT 98:34596
GI



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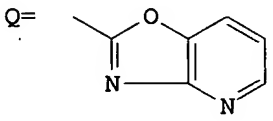
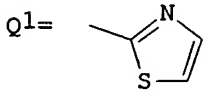
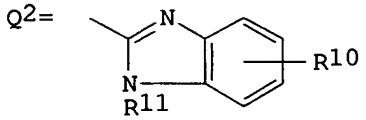
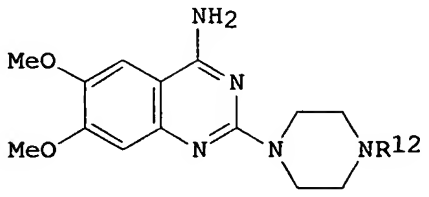








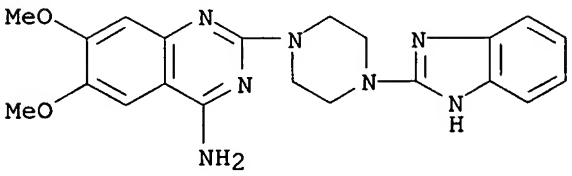
II

AB The antihypertensive (no data) title compds. I [R1,R2 = H, R1R2 = CR6:CR7CR8:CR9 (R6-R9 = H, alkoxy; R3 = Q, Q1, Q2 (R10 = H, halo, alkyl, alkoxy, HO, 1-oxoalkoxy, amino, alkylamino, dialkylamino; R11 = alkyl); R4, R5 = H, alkyl, n = 1, 2] and their therapeutically acceptable and addn. salts were prepd. Thus, 4-amino-6,7-dimethoxy-2-(1-piperazinyl)quinazoline-HCl was treated with 2-chlorobenzimidazole to give the piperazinoquinazolinamine II (R12 = 2-benzimidazolyl). 2-Piperazinocycloheptimidazole-HCl prepd. from methoxy-2,4,6-cyclohexatatriene, was treated with 2-chloro-4-amino-6,7-dimethoxyquinazoline to give II (R12 = 2-cycloheptimidazolyl).

IT **80841-32-3P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 80841-32-3 CAPLUS

CN 4-Quinazolinamine, 2-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-6,7-dimethoxy- (9CI) (CA INDEX NAME)



L4 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1982:85588 CAPLUS

DN 96:85588

TI 2-(1-Piperazinyl)-4-pyrimidinamines and related compounds

IN Rakhit, Sumanas; Bagli, Jehan Framroz

PA American Home Products Corp., USA

SO Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW

DT Patent

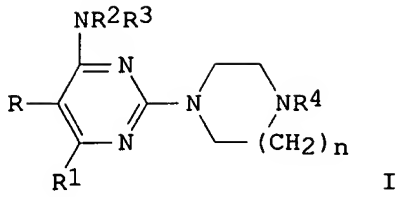
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 39190	A1	19811104	EP 1981-301719	19810416
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4333937	A	19820608	US 1980-141548	19800418
	US 4351832	A	19820928	US 1981-245798	19810320
	AU 8170789	A1	19811110	AU 1981-70789	19810416
	JP 57500561	T2	19820401	JP 1981-501442	19810416
	DK 8105624	A	19811217	DK 1981-5624	19811217
PRAI	US 1980-141548	A	19800418		
	US 1981-245798	A	19810320		
	WO 1981-US502	A	19810416		

OS CASREACT 96:85588

GI



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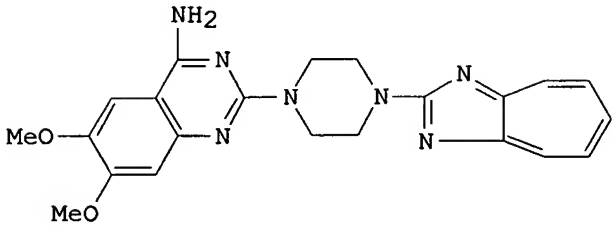


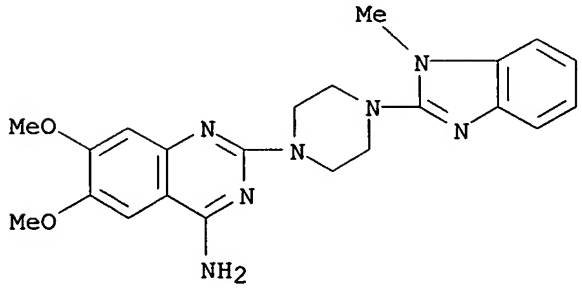
III

AB The title compds. I [R, R1 = H; RR1 = (un)substituted CH:CHCH:CH; R2,R3 = H, alkyl, R4 = (un)substituted pyridooxazolyl,thiazolyl, cycloheptaimidazolyl, oxocycloheptyl, benzoxazolyl, benzothiazolyl, benzimidazolyl; n = 1,2] were prepd. Thus, 2-(1-piperazinyl)cycloheptimidazole (II) was prepd. by treating formylpiperazine with MeSC(:NH)NH2 and 2-methoxy-2,4,6-cycloheptatrienone, followed by deformylation. Treatment of II with 4-amino-2-chloro-6,7-dimethoxyquinazoline gave III, which at 1 mg/kg orally in rats gave a 20% decrease in blood pressure.

IT **80841-34-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antihypertensive activity of)

RN 80841-34-5 CAPLUS

CN 4-Quinazolinamine, 6,7-dimethoxy-2-[4-(1-methyl-1H-benzimidazol-2-yl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	103.07	301.13

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                                                     ENTRY    SESSION
CA SUBSCRIBER PRICE                                 -14.25     -14.25

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FILE COVERS 1907-1966
FILE LAST UPDATED:  01 May 1997 (19970501/UP)

  This file contains CAS Registry Numbers for easy and accurate
  substance identification.  Title keywords, authors, patent
  assignees, and patent information, e.g., patent numbers, are
  now searchable from 1907-1966.  TIFF images of CA abstracts
  printed between 1907-1966 are available in the PAGE
  display formats.

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  This file supports REG1stRY for direct browsing and searching of
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  more information.

=> d his

     (FILE 'HOME' ENTERED AT 12:50:53 ON 16 FEB 2006)

     FILE 'REGISTRY' ENTERED AT 12:52:18 ON 16 FEB 2006
L1              STRUCTURE UPLOADED
L2           15 S L1
L3          429 S L1 SSS FULL
                SAVE L3 TEN688246/A

     FILE 'CAPLUS' ENTERED AT 12:55:38 ON 16 FEB 2006
L4           19 S L3

     FILE 'CAOLD' ENTERED AT 13:03:26 ON 16 FEB 2006

=> s l3
L5            0 L3

=> file caplus
COST IN U.S. DOLLARS                              SINCE FILE      TOTAL
                                                     ENTRY    SESSION
FULL ESTIMATED COST                                   4.40     305.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)        SINCE FILE      TOTAL
                                                     ENTRY    SESSION
CA SUBSCRIBER PRICE                                   0.00     -14.25

FILE 'CAPLUS' ENTERED AT 13:09:09 ON 16 FEB 2006
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FILE COVERS 1907 - 16 Feb 2006 VOL 144 ISS 8
FILE LAST UPDATED: 15 Feb 2006 (20060215/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html

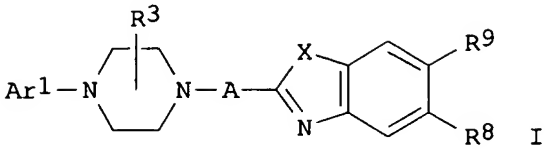
=> d l4 6 8-19 bib abs hitstr

L4 ANSWER 6 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:566601 CAPLUS
DN 141:123640
TI Heterocyclylpiperazinylbenzothiazoles, heterocyclylpiperazinylbenzimidazoles, and heterocyclylpiperazinylbenzooxazoles prepared as antagonists for the metabotropic glutamate receptors mGluR1 and mGluR5 and as ligands for human VR1
IN Sun, Qun; Tafesse, Laykea; Victory, Sam
PA Euro-Celtique S.A., Luxembourg
SO PCT Int. Appl., 705 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2004058754	A1	20040715	WO 2003-US41100	20031222
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
	RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	US 2004186111	A1	20040923	US 2003-739190	20031219
	CA 2511509	AA	20040715	CA 2003-2511509	20031222
	EP 1583763	A1	20051012	EP 2003-814351	20031222
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
	BR 2003017757	A	20051122	BR 2003-17757	20031222
	NO 2005003582	A	20050907	NO 2005-3582	20050722
PRAI	US 2002-435917P	P	20021224		
	US 2003-459626P	P	20030403		
	US 2003-473856P	P	20030529		
	WO 2003-US41100	W	20031222		

OS MARPAT 141:123640
GI

OS MARPAT 141:123640
GI



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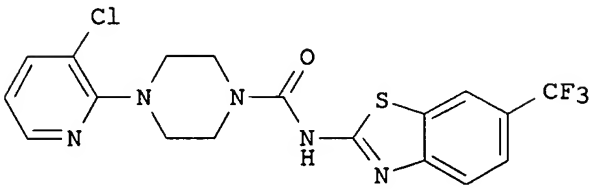
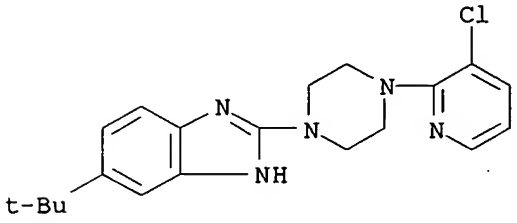


II

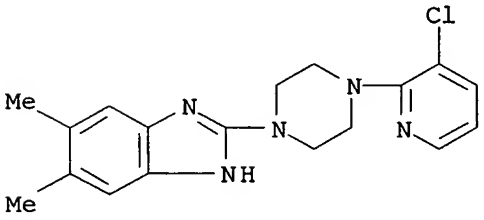
AB Heterocyclylpiperazinyl benzothiazoles, benzimidazoles, and benzooxazoles I [A = bond, C(:O)NR4, C(:S)NR4; Ar1 = (un)substituted pyridinyl, pyrazinyl, thiadiazolyl, pyrimidinyl, or pyridazinyl; R3 = H, Me, halogen, cyano, hydroxy, alkoxy, nitro, amino, etc.; X = S, O, NR10; R8, R9 = H, alkyl, alkenyl, alkynyl, cycloalkyl, Ph, halo, halomethyl, dihalomethyl, trihalomethyl, cyano, etc.; R10 = H, alkyl] such as II are prepd. as antagonists for the metabotropic glutamate receptors mGluR1 and mGluR5 and as ligands for the protein VR1 for the treatment of pain, addiction, urinary incontinence, irritable-bowel disorder, inflammatory bowel disease, ulcers, Parkinson's disease, epilepsy, seizures, anxiety, psychosis, stroke, pruritus, cognitive disorders, memory deficits or restricted brain function, Huntington's chorea, amyotrophic lateral sclerosis, retinopathy, muscle spasms, migraines, vomiting, dyskinesia, and depression. Regioselective coupling of 2,3-dichloropyridine and piperazine yields 1-(3-chloro-2-pyridinyl)piperazine (III), while acylation of 6-(trifluoromethyl)-2-aminobenzothiazole with p-nitrophenyl chlorocarbonate yields p-nitrophenyl [6-(trifluoromethyl)-2-benzothiazolyl]carbamate (IV); coupling of III and IV yields II. II gives IC50 values of 262 and 51 (units not indicated) in pH-based and capsaicin-based assays (resp.) for binding to human VR1.

IT **722497-97-4P 722497-98-5P 722497-99-6P**
722498-00-2P 722498-01-3P 722498-02-4P
722498-03-5P 722498-04-6P 722498-05-7P
722498-06-8P 722498-09-1P 722498-10-4P
722498-11-5P 722498-12-6P 722498-13-7P
722498-14-8P 722498-23-9P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(drug candidate; prepn. of (heterocyclylpiperazinyl)benzothiazoles, benzimidazoles, and benzooxazoles as metabotropic glutamate receptor antagonists and as ligands for VR1 in treatment of disorders such as addiction and pain)

RN 722497-97-4 CAPLUS
CN 1H-Benzimidazole, 2-[4-(3-chloro-2-pyridinyl)-1-piperazinyl]-5-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

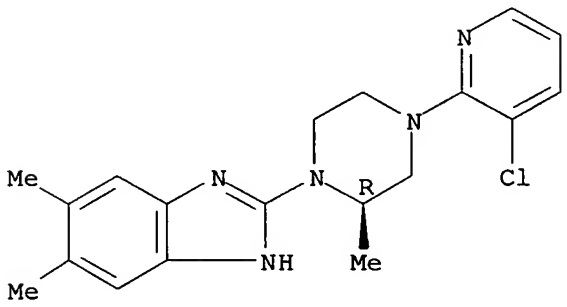


RN 722497-98-5 CAPLUS
CN 1H-Benzimidazole, 2-[4-(3-chloro-2-pyridinyl)-1-piperazinyl]-5,6-dimethyl- (9CI) (CA INDEX NAME)



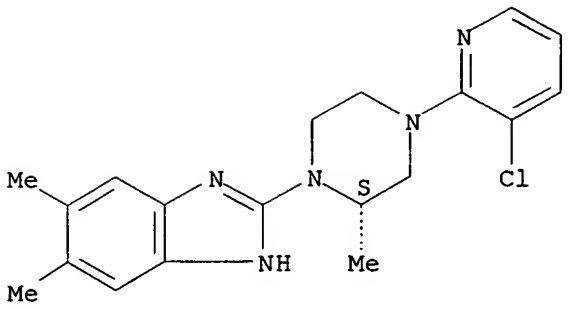
RN 722497-99-6 CAPLUS
CN 1H-Benzimidazole, 2-[(2R)-4-(3-chloro-2-pyridinyl)-2-methyl-1-piperazinyl]-5,6-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



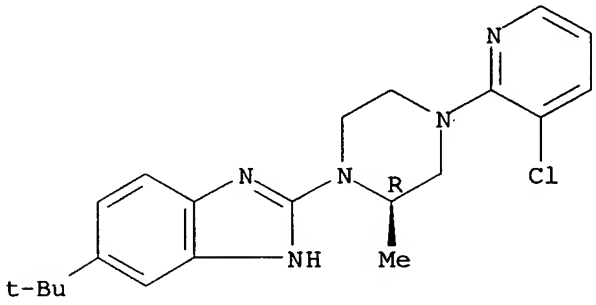
RN 722498-00-2 CAPLUS
CN 1H-Benzimidazole, 2-[(2S)-4-(3-chloro-2-pyridinyl)-2-methyl-1-piperazinyl]-5,6-dimethyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

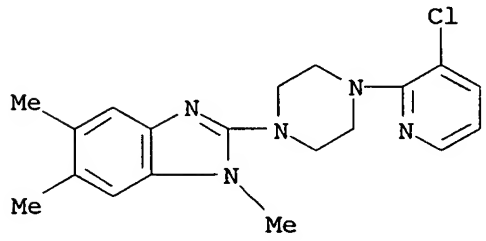


RN 722498-01-3 CAPLUS
CN 1H-Benzimidazole, 2-[(2R)-4-(3-chloro-2-pyridinyl)-2-methyl-1-piperazinyl]-5-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

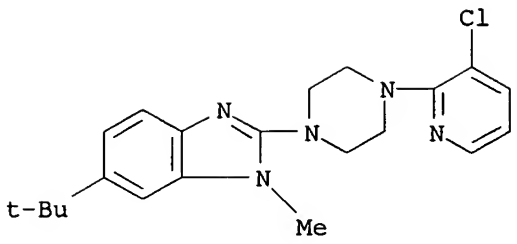
Absolute stereochemistry.



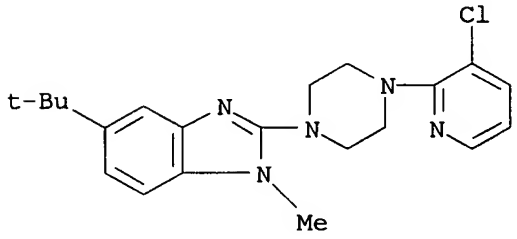
RN 722498-02-4 CAPLUS
CN 1H-Benzimidazole, 2-[4-(3-chloro-2-pyridinyl)-1-piperazinyl]-1,5,6-trimethyl- (9CI) (CA INDEX NAME)



RN 722498-03-5 CAPLUS
CN 1H-Benzimidazole, 2-[4-(3-chloro-2-pyridinyl)-1-piperazinyl]-6-(1,1-dimethylethyl)-1-methyl- (9CI) (CA INDEX NAME)

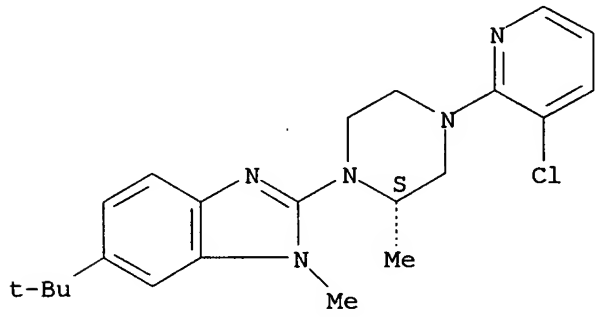


RN 722498-04-6 CAPLUS
CN 1H-Benzimidazole, 2-[4-(3-chloro-2-pyridinyl)-1-piperazinyl]-5-(1,1-dimethylethyl)-1-methyl- (9CI) (CA INDEX NAME)



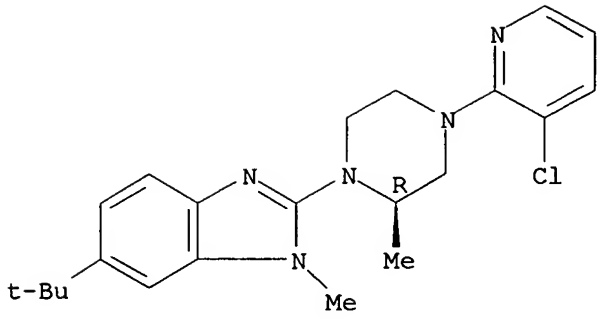
RN 722498-05-7 CAPLUS
CN 1H-Benzimidazole, 2-[(2S)-4-(3-chloro-2-pyridinyl)-2-methyl-1-piperazinyl]-6-(1,1-dimethylethyl)-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



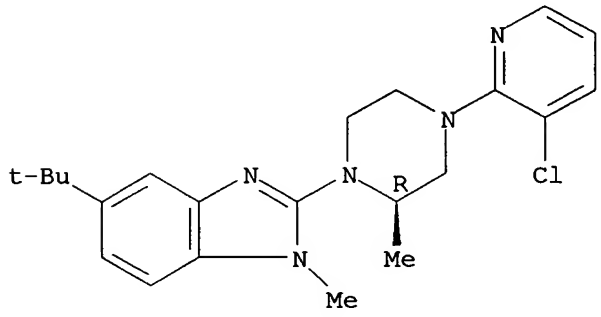
RN 722498-06-8 CAPLUS
CN 1H-Benzimidazole, 2-[(2R)-4-(3-chloro-2-pyridinyl)-2-methyl-1-piperazinyl]-6-(1,1-dimethylethyl)-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



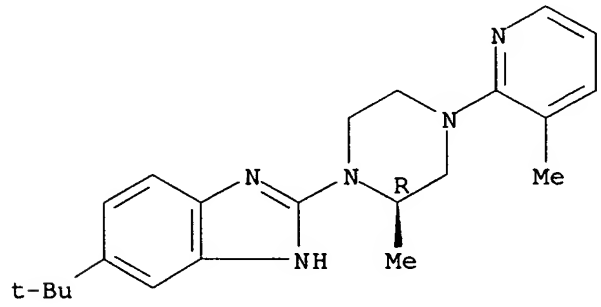
RN 722498-09-1 CAPLUS
CN 1H-Benzimidazole, 2-[(2R)-4-(3-chloro-2-pyridinyl)-2-methyl-1-piperazinyl]-5-(1,1-dimethylethyl)-1-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



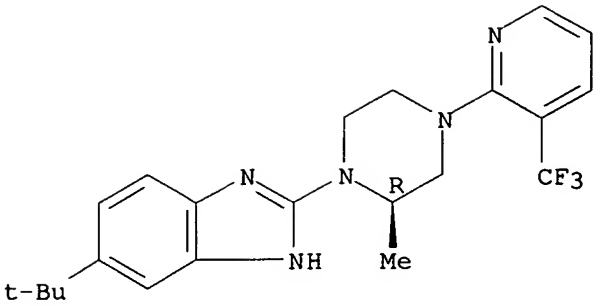
RN 722498-10-4 CAPLUS
CN 1H-Benzimidazole, 5-(1,1-dimethylethyl)-2-[(2R)-2-methyl-4-(3-methyl-2-pyridinyl)-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



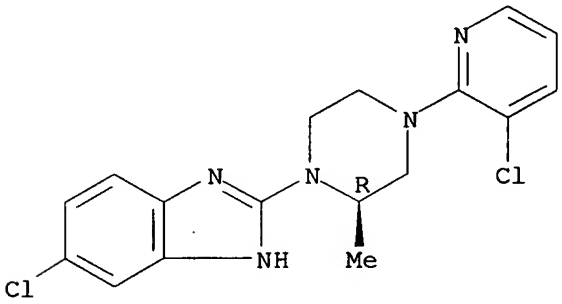
RN 722498-11-5 CAPLUS
CN 1H-Benzimidazole, 5-(1,1-dimethylethyl)-2-[(2R)-2-methyl-4-[3-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



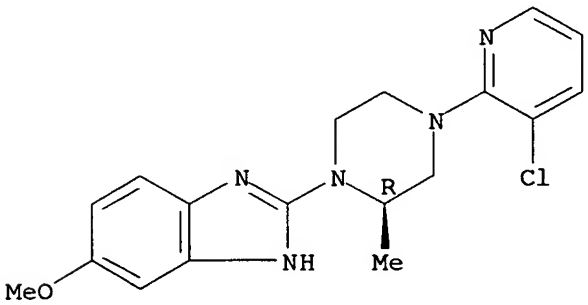
RN 722498-12-6 CAPLUS
CN 1H-Benzimidazole, 5-chloro-2-[(2R)-4-(3-chloro-2-pyridinyl)-2-methyl-1-piperazinyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



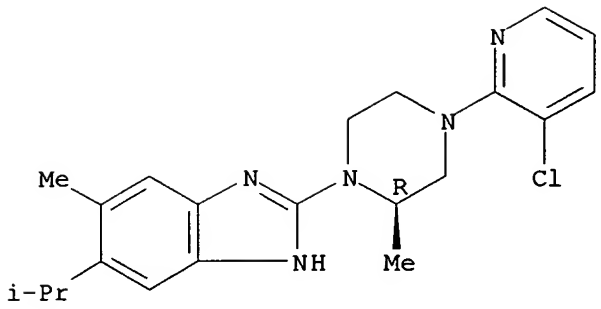
RN 722498-13-7 CAPLUS
CN 1H-Benzimidazole, 2-[(2R)-4-(3-chloro-2-pyridinyl)-2-methyl-1-piperazinyl]-5-methoxy- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



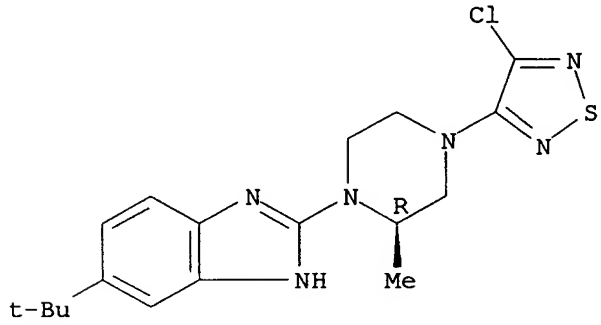
RN 722498-14-8 CAPLUS
CN 1H-Benzimidazole, 2-[(2R)-4-(3-chloro-2-pyridinyl)-2-methyl-1-piperazinyl]-5-methyl-6-(1-methylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 722498-23-9 CAPLUS
CN 1H-Benzimidazole, 2-[(2R)-4-(4-chloro-1,2,5-thiadiazol-3-yl)-2-methyl-1-piperazinyl]-5-(1,1-dimethylethyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L4 ANSWER 8 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2004:20661 CAPLUS
DN 140:93938
TI Preparation of substituted quinolines useful as CCR5 receptor antagonists
IN Dunning, Laura; Jaroch, Stefan; Kochanny, Monica J.; Lee, Wheeseong; Lian, Xiongdong; Liang, Meina; Lu, Shou-Fu; Onuffer, James; Phillips, Gary; Wei, Guo-Ping; Ye, Bin
PA Schering Aktiengesellschaft, Germany
SO PCT Int. Appl., 241 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004002960	A1	20040108	WO 2003-US20950	20030624

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,

	FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	CA 2489560	AA	20040108	CA 2003-2489560 20030624
	BR 2003012204	A	20050426	BR 2003-12204 20030624
	EP 1534681	A1	20050601	EP 2003-762325 20030624
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK			
	JP 2005537247	T2	20051208	JP 2004-518228 20030624
	US 2004072818	A1	20040415	US 2003-607530 20030626
	NO 2005000429	A	20050329	NO 2005-429 20050126
PRAI	US 2002-451687P	P	20020627	
	WO 2003-US20950	W	20030624	
OS	MARPAT 140:93938			
GI				

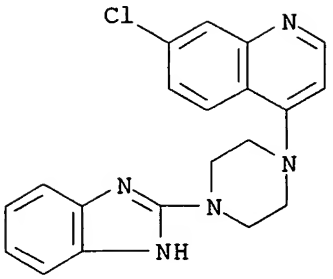
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The present invention relates to quinoline derivs. of formula I and II [wherein: R1, R1* = H, (un)substituted amino, alkyl, haloalkyl, OH, alkoxy, CO2R9a; R2, R2*, R3, R3* = H, (halo)alkyl, halogen, (un)substituted amino, nitro, cyano, alkoxy; R4, R4* = H, alkyl; R5 = H, R9, R9-aminocycloalk(en)yl, (alk/aryl)oxycarbonyl, SO2R9, C(O)NR7R9, C(O)NR7-SO2R9, C(O)R6, C(O)R9, C(=NR10)R9, C(S)R9, C(=NR10)NHR9, C(S)NHR9, C(S)NR7-SO2R9; R6 is a group of formula III; R7, R7* = H, (un)substituted alkyl or aryl; R9a = arylalkyl, cycloalk(en)yl, cycloalkylalkyl, alkyl, heterocyclylalkyl, aryl, heterocyclyl any of which can be (un)substituted; R9 is same as R9a except H; R10 = H, cyano, (un)substituted alkyl or alkoxy; n = 0-3, n* = 1-3], their enantiomers, diastereomers, salts, and solvates. For instance, quinoline IV was prepd. via amination of 4,7-dichloroquinoline by piperazine, and subsequent addn. of obtained 7-chloro-4-(piperazin-1-yl)quinoline to 4-FC6H4NCO. The invention compds. are claimed as CCR5 receptor antagonists (no data) and useful for treating the CCR5-mediated inflammatory and immunoregulatory disorders such as optic neuritis, stroke, dermatitis, HIV, diabetes, etc.

IT **643042-39-1P**, 4-[4-(Benzimidazol-2-yl)piperazin-1-yl]-7-chloroquinoline
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of quinoline derivs. useful as CCR5 receptor antagonists)

RN 643042-39-1 CAPLUS

CN Quinoline, 4-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-7-chloro- (9CI) (CA INDEX NAME)



RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2003:539807 CAPLUS
DN 139:69267
TI Preparation of 2-benzimidazolylamines as ORL1-receptor agonists for the treatment of pain and inflammatory diseases
IN Ito, Fumitaka
PA Pfizer Inc., USA
SO Eur. Pat. Appl., 33 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 1069124	A1	20010117	EP 2000-305981	20000714
	EP 1069124	B1	20040512		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	US 6340681	B1	20020122	US 2000-606921	20000629
	JP 2001048879	A2	20010220	JP 2000-209374	20000711
	JP 3276111	B2	20020422		
	JP 2001039974	A2	20010213	JP 2000-211264	20000712
	BR 2000002796	A	20010403	BR 2000-2796	20000714
	AT 266657	E	20040515	AT 2000-305981	20000714
	PT 1069124	T	20040930	PT 2000-305981	20000714
	ES 2219272	T3	20041201	ES 2000-305981	20000714
	CA 2314008	AA	20010116	CA 2000-2314008	20000717
PRAI	WO 1999-IB1290	W	19990716		

OS MARPAT 139:69267
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1, R2 = H, halo, OH, etc.; R3, R4 = H, halo-alkyl, substituted alkyl, i.e., OH, alkoxy, alkyl-S, etc.; R5 = pheny, substituted cycloalkyl, i.e., H, halo, OH, etc.;] and their pharmaceutically acceptable salts were prepd. For example, N-alkylation of N-methylpiperazine by chlorobenzimidazolyl II, e.g., prepd. from 1,3-dihydro-1-(4-piperidinyl)-2H-benzimidazol-2-one in 2-steps, afforded

2-benzimidazolylamine III in 15% yield. In selective affinity studies of opioid receptors, i.e., ORL1, .mu., .kappa. and .delta., some examples of compds. I exhibited good ORL1-receptor agonist activity. Compds. I are claimed useful as analgesics.

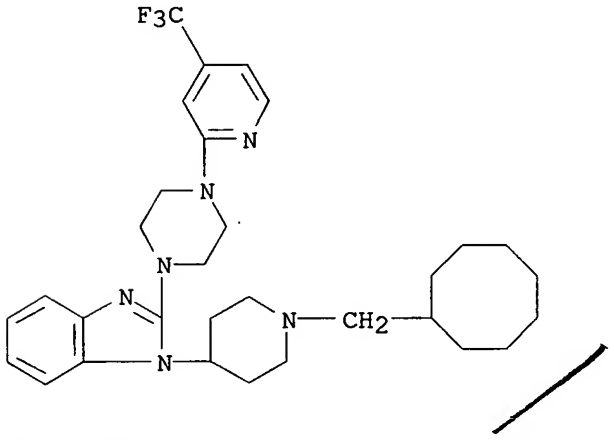
IT **548794-06-5P 548794-07-6P 548794-08-7P 548794-09-8P**

RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(target compd.; prepn. of 2-benzimidazolylamines as ORL1-receptor agonists for the treatment of pain and inflammatory diseases)

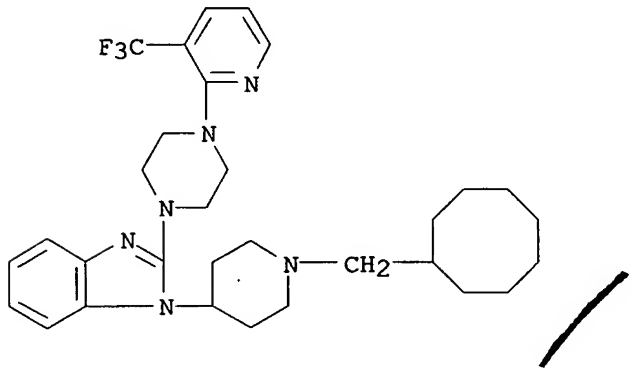
RN 548794-06-5 CAPLUS

CN 1H-Benzimidazole, 1-[1-(cyclooctylmethyl)-4-piperidinyl]-2-[4-[4-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



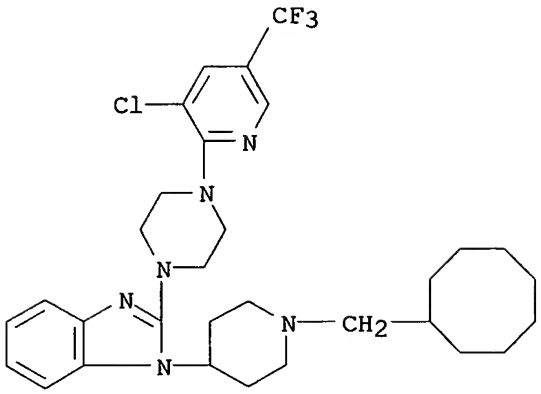
RN 548794-07-6 CAPLUS

CN 1H-Benzimidazole, 1-[1-(cyclooctylmethyl)-4-piperidinyl]-2-[4-[3-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

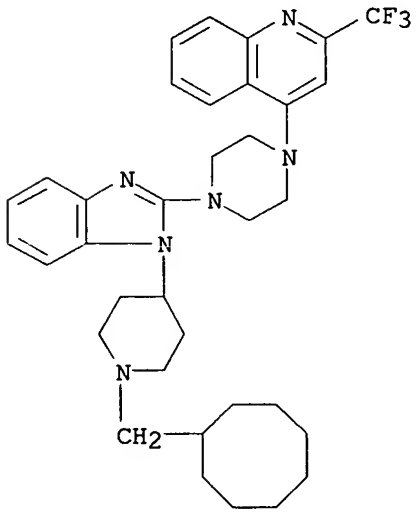


RN 548794-08-7 CAPLUS

CN 1H-Benzimidazole, 2-[4-[3-chloro-5-(trifluoromethyl)-2-pyridinyl]-1-piperazinyl]-1-[1-(cyclooctylmethyl)-4-piperidinyl]- (9CI) (CA INDEX NAME)



RN 548794-09-8 CAPLUS
CN Quinoline, 4-[4-[1-[1-(cyclooctylmethyl)-4-piperidinyl]-1H-benzimidazol-2-yl]-1-piperazinyl]-2-(trifluoromethyl)- (9CI) (CA INDEX NAME)

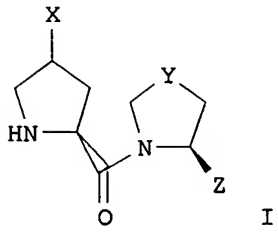


RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2002:142666 CAPLUS
DN 136:200479
TI Preparation of proline derivatives as dipeptidyl peptidase IV (DPP-IV) inhibitors and use thereof as drugs
IN Kitajima, Hiroshi; Sakashita, Hiroshi; Akahoshi, Fumihiko; Hayashi, Yoshiharu
PA Welfide Corporation, Japan
SO PCT Int. Appl., 340 pp.
CODEN: PIXXD2
DT Patent
LA Japanese
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002014271	A1	20020221	WO 2001-JP6906	20010810
	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
	RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
	CA 2418656	AA	20020221	CA 2001-2418656	20010810
	AU 2001077754	A5	20020225	AU 2001-77754	20010810
	EP 1308439	A1	20030507	EP 2001-955660	20010810
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
	BR 2001013146	A	20030624	BR 2001-13146	20010810
	NZ 524618	A	20040827	NZ 2001-524618	20010810
	NO 2003000619	A	20030226	NO 2003-619	20030207
	US 2004106655	A1	20040603	US 2003-344255	20030210
	US 2005245538	A1	20051103	US 2005-142523	20050602
PRAI	JP 2000-243217	A	20000810		
	JP 2000-400296	A	20001228		
	WO 2001-JP6906	W	20010810		
	US 2003-344255	A3	20030210		
OS	MARPAT 136:200479				

GI



I

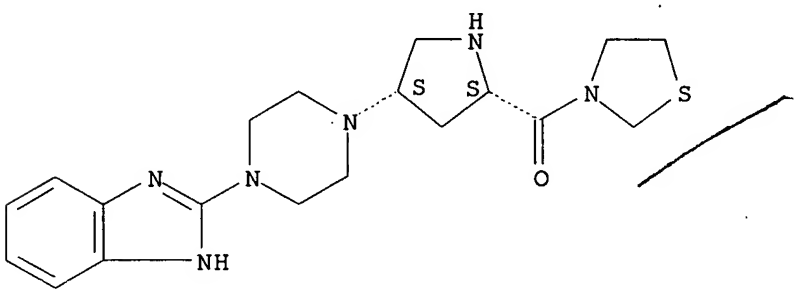
AB The title compds. [I; X = NR1R2, NR3COR4, NR5COR4, NR5CH2CH2NR6R7, NR8SO2R9, OR10, O2CR11; wherein R1, R2 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, heteroarylalkyl, or they are linked to each other to form a heterocyclyl contg. 1 or 2 N atoms or O which may be a spiro ring and is optionally fused to an (un)substituted arom. ring; R3, R4 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, arylalkenyl, heteroaryl, heteroarylalkyl; R5, R6, R7 = H, alkyl, acyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl, or which is optionally fused to an (un)substituted arom. ring; R8, R9, R10, R11 = H, alkyl, cycloalkyl, cycloalkylalkyl, aryl, arylalkyl, heteroaryl, or heteroarylalkyl] or pharmacol. acceptable salts thereof are prepd. These compds. are useful for the treatment of DPP-IV related diseases such as diabetes, obesity, HIV infection, cancer metastasis, skin diseases, prostatic hypertrophy (prostatomegaly), pericementitis, or autoimmune diseases. Thus, a soln. of 0.924 g (S)-1-[(2S,4S)-4-amino-1-tert-butoxycarbonyl-2-pyrrolidinylcarbonyl]-2-cyanopyrrolidine (prepn. given), 1.7 mL diisopropylethylamine, and 0.78 g

2-chloro-4-fluorobenzonitrile in 10 mL N-methyl-2-pyrrolidone were stirred at 80.degree. for 4 h to give 0.94 g (S)-1-[(2S,4S)-1-tert-butoxycarbonyl-4-(3-chloro-4-cyanophenyl)amino-2-pyrrolidinylcarbonyl]-2-cyanopyrrolidine which (0.93 g) was treated with HCl/EtOAc at room temp. for 15 h to give (S)-1-[(2S,4S)-4-(3-chloro-4-cyanophenyl)amino-2-pyrrolidinylcarbonyl]-2-cyanopyrrolidine hydrochloride (II). II showed IC50 of 0.13 and 0.15 nM against human blood plasma DPP-IV and rat blood plasma DPP-IV, resp.

IT **401563-25-5P 401563-26-6P 401563-27-7P**
401563-28-8P 401563-29-9P 401563-30-2P
401563-31-3P 401563-32-4P 401563-33-5P
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of proline derivs. as dipeptidyl peptidase IV (DPP-IV) inhibitors for treating DPP-IV related diseases)

RN 401563-25-5 CAPLUS
CN Thiazolidine, 3-[[(2S,4S)-4-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, dihydrochloride (9CI) (CA INDEX NAME)

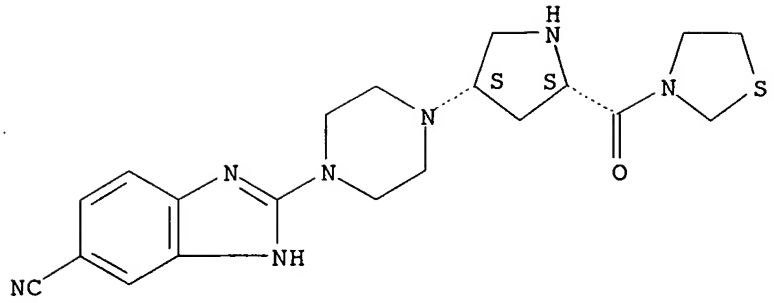
Absolute stereochemistry.



●2 HCl

RN 401563-26-6 CAPLUS
CN Thiazolidine, 3-[[(2S,4S)-4-[4-(5-cyano-1H-benzimidazol-2-yl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, trihydrochloride (9CI) (CA INDEX NAME)

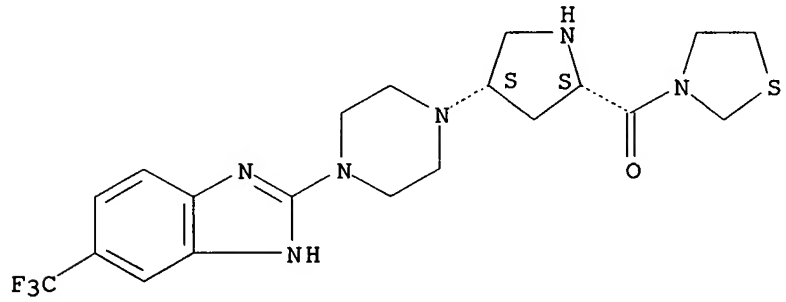
Absolute stereochemistry.



●3 HCl

RN 401563-27-7 CAPLUS
CN Thiazolidine, 3-[[(2S,4S)-4-[4-[5-(trifluoromethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, trihydrobromide (9CI) (CA INDEX NAME)

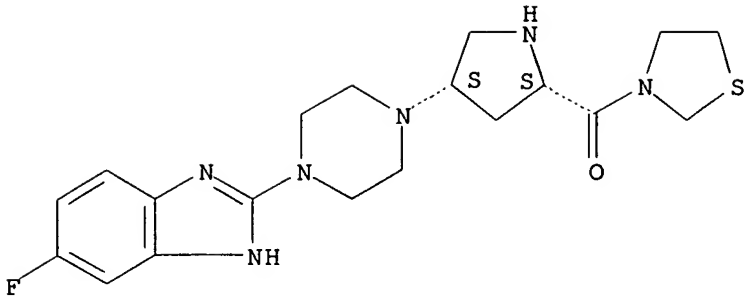
Absolute stereochemistry.



●3 HBr

RN 401563-28-8 CAPLUS
CN Thiazolidine, 3-[[(2S,4S)-4-[4-(5-fluoro-1H-benzimidazol-2-yl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, trihydrobromide (9CI) (CA INDEX NAME)

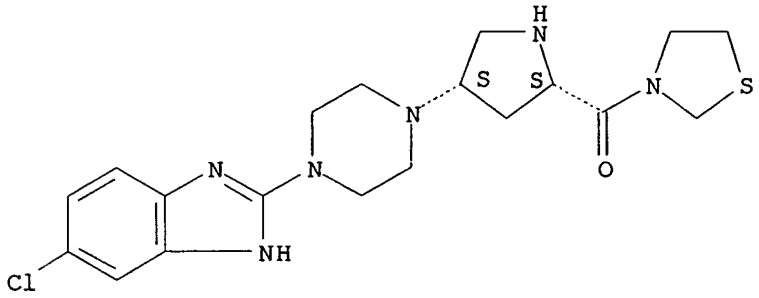
Absolute stereochemistry.



●3 HBr

RN 401563-29-9 CAPLUS
CN Thiazolidine, 3-[[(2S,4S)-4-[4-(5-chloro-1H-benzimidazol-2-yl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, trihydrobromide (9CI) (CA INDEX NAME)

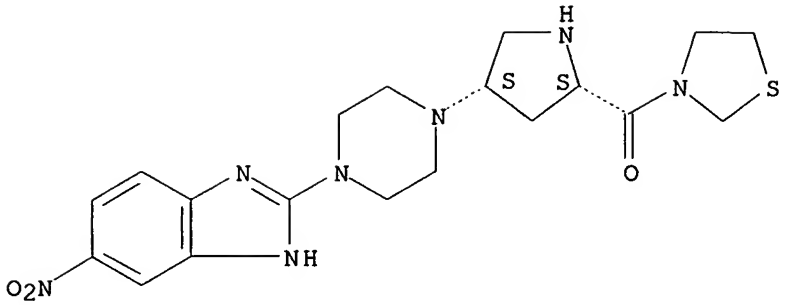
Absolute stereochemistry.



●3 HBr

RN 401563-30-2 CAPLUS
CN Thiazolidine, 3-[[(2S,4S)-4-[4-(5-nitro-1H-benzimidazol-2-yl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, trihydrochloride (9CI) (CA INDEX NAME)

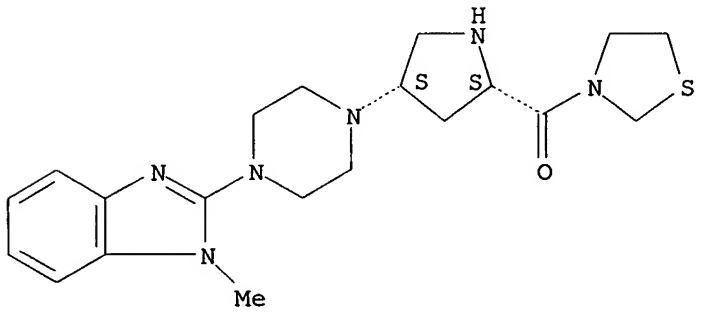
Absolute stereochemistry.



● 3 HCl

RN 401563-31-3 CAPLUS
CN Thiazolidine, 3-[[(2S,4S)-4-[4-(1-methyl-1H-benzimidazol-2-yl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, trihydrochloride (9CI) (CA INDEX NAME)

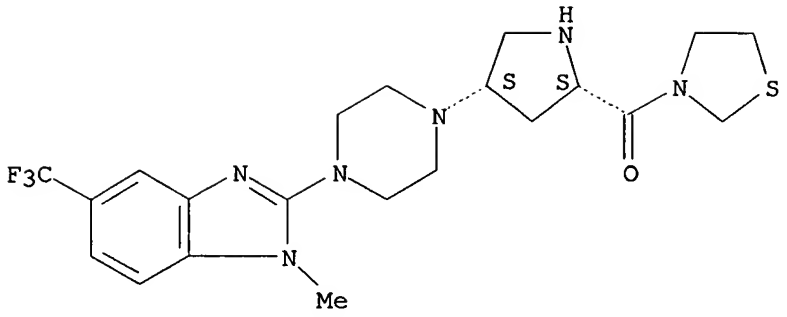
Absolute stereochemistry.



● 3 HCl

RN 401563-32-4 CAPLUS
CN Thiazolidine, 3-[[(2S,4S)-4-[4-[1-methyl-5-(trifluoromethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, trihydrochloride (9CI) (CA INDEX NAME)

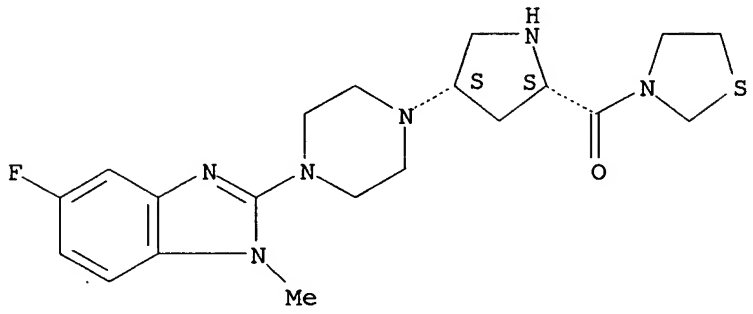
Absolute stereochemistry.



●3 HCl

RN 401563-33-5 CAPLUS
CN Thiazolidine, 3-[[(2S,4S)-4-[4-(5-fluoro-1-methyl-1H-benzimidazol-2-yl)-1-piperazinyl]-2-pyrrolidinyl]carbonyl]-, trihydrochloride (9CI) (CA INDEX NAME)

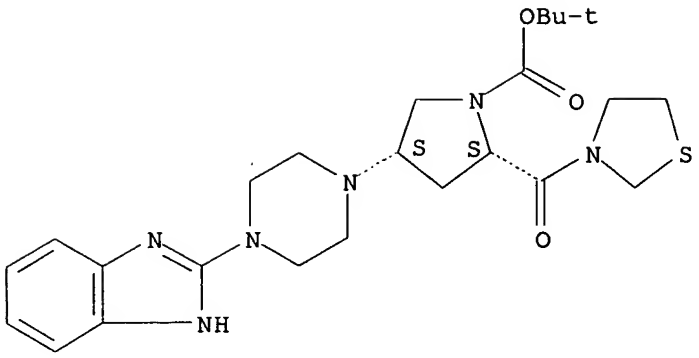
Absolute stereochemistry.



●3 HCl

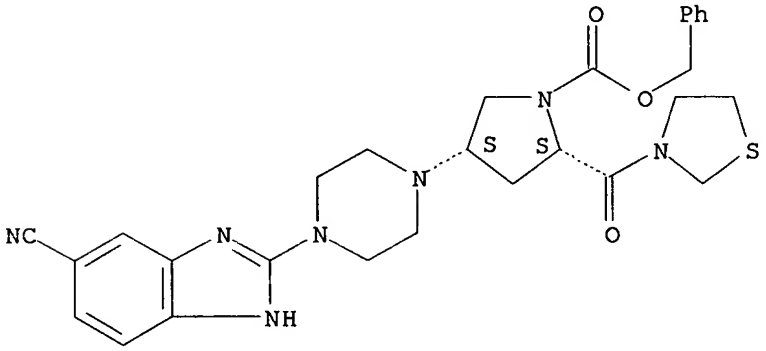
IT **401566-99-2P 401567-01-9P 401567-02-0P**
401567-03-1P 401567-04-2P 401567-06-4P
401567-07-5P 401567-09-7P 401567-13-3P
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of proline derivs. as dipeptidyl peptidase IV (DPP-IV) inhibitors for treating DPP-IV related diseases)
RN 401566-99-2 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-2-(3-thiazolidinylcarbonyl)-, 1,1-dimethylethyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



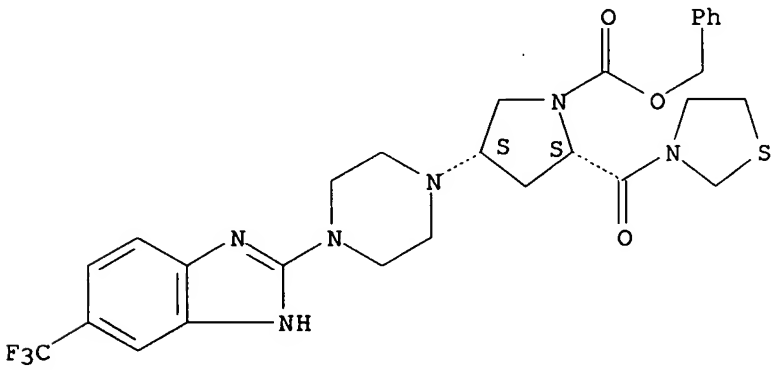
RN 401567-01-9 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-[4-(5-cyano-1H-benzimidazol-2-yl)-1-piperazinyl]-2-(3-thiazolidinylcarbonyl)-, phenylmethyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



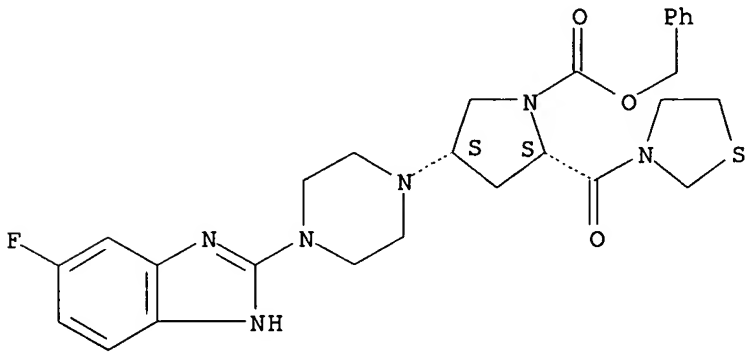
RN 401567-02-0 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 2-(3-thiazolidinylcarbonyl)-4-[4-[5-(trifluoromethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]-, phenylmethyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



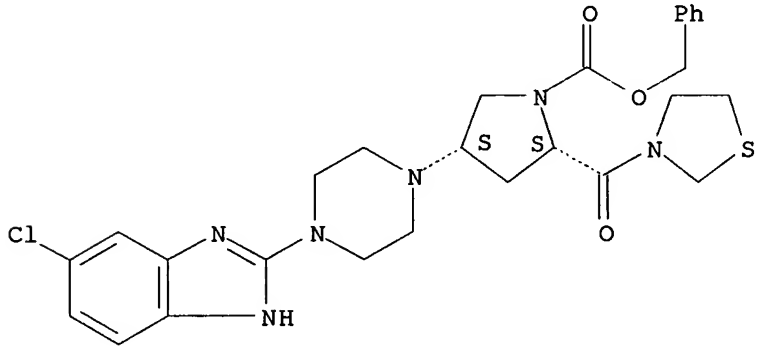
RN 401567-03-1 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-[4-(5-fluoro-1H-benzimidazol-2-yl)-1-piperazinyl]-2-(3-thiazolidinylcarbonyl)-, phenylmethyl ester, (2S,4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



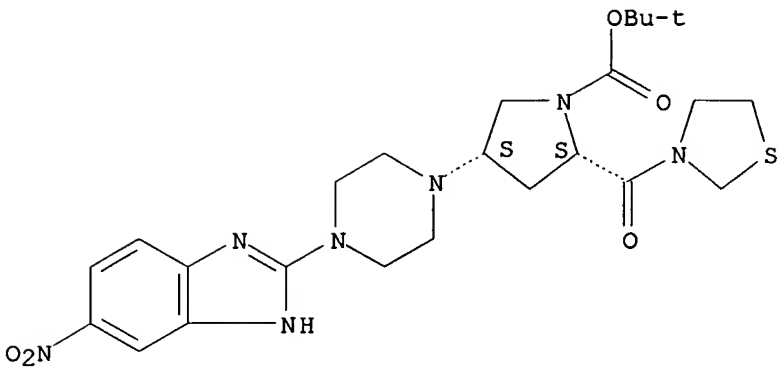
RN 401567-04-2 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-[4-(5-chloro-1H-benzimidazol-2-yl)-1-piperazinyl]-2-(3-thiazolidinylcarbonyl)-, phenylmethyl ester, (2S,4S)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



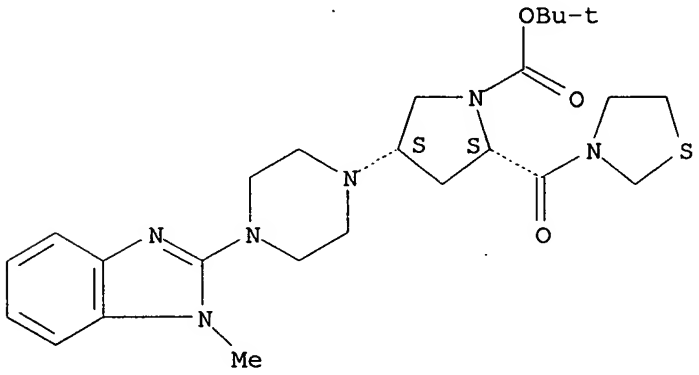
RN 401567-06-4 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-[4-(5-nitro-1H-benzimidazol-2-yl)-1-piperazinyl]-2-(3-thiazolidinylcarbonyl)-, 1,1-dimethylethyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



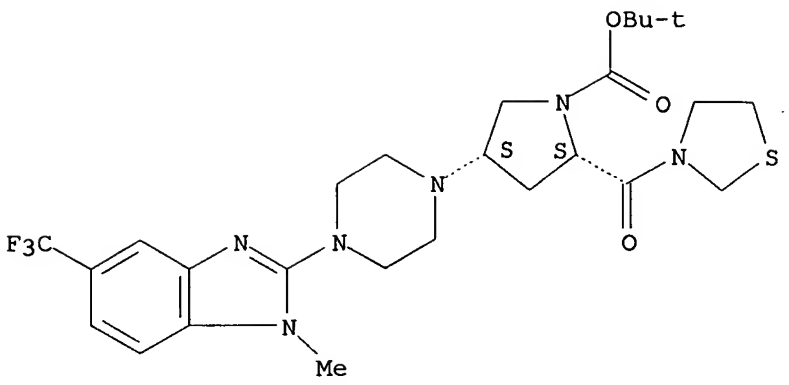
RN 401567-07-5 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-[4-(1-methyl-1H-benzimidazol-2-yl)-1-piperazinyl]-2-(3-thiazolidinylcarbonyl)-, 1,1-dimethylethyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



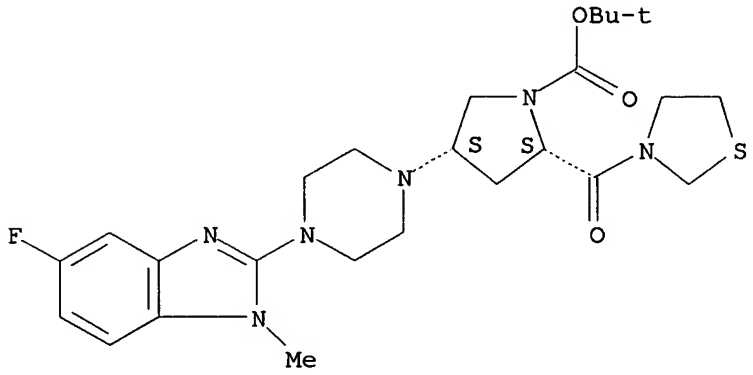
RN 401567-09-7 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-[4-[1-methyl-5-(trifluoromethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]-2-(3-thiazolidinylcarbonyl)-, 1,1-dimethylethyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 401567-13-3 CAPLUS
CN 1-Pyrrolidinecarboxylic acid, 4-[4-(5-fluoro-1-methyl-1H-benzimidazol-2-yl)-1-piperazinyl]-2-(3-thiazolidinylcarbonyl)-, 1,1-dimethylethyl ester, (2S,4S)- (9CI) (CA INDEX NAME)

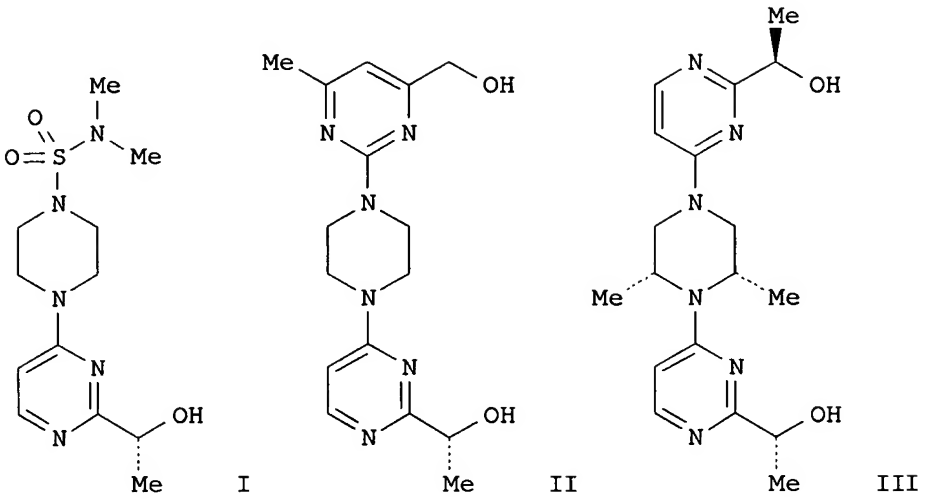
Absolute stereochemistry.



RE.CNT 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2001:916027 CAPLUS
DN 136:200160
TI Orally-Effective, Long-Acting Sorbitol Dehydrogenase Inhibitors: Synthesis, Structure-Activity Relationships, and in Vivo Evaluations of Novel Heterocycle-Substituted Piperazino-Pyrimidines
AU Chu-Moyer, Margaret Y.; Ballinger, William E.; Beebe, David A.; Berger, Richard; Coutcher, James B.; Day, Wesley W.; Li, Jiancheng; Mylari, Banavara L.; Oates, Peter J.; Weekly, R. Matthew
CS Departments of Cardiovascular and Metabolic Disease and Drug Metabolism Development, Pfizer Global Research and Development, Groton Laboratories, Groton, CT, 06340, USA
SO Journal of Medicinal Chemistry (2002), 45(2), 511-528
CODEN: JMCMAR; ISSN: 0022-2623
PB American Chemical Society
DT Journal
LA English

OS CASREACT 136:200160
GI



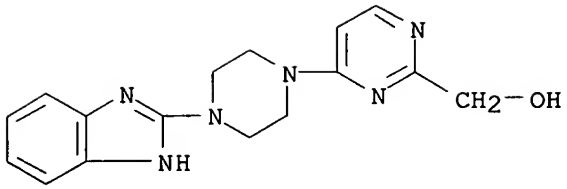
I II III

AB Optimization of a previously disclosed sorbitol dehydrogenase inhibitor (SDI, I) for potency and duration of action was achieved by replacing the metabolically labile N,N-dimethylsulfamoyl group with a variety of heterocycles. Specifically, this effort led to a series of novel, in vitro potent SDI's, e.g. the [[(hydroxymethylpyrimidinyl)piperazinyl]pyrimidinyl]ethanol II, with longer serum half-lives and acceptable in vivo activity in acutely diabetic rats. However, the desired in vivo potency in chronically diabetic rats, ED90 .ltoreq. 5 mg/kg/day, was achieved only through further modification of the piperazine linker. Several members of this family, including [[(hydroxyethylpyrimidinyl)dimethylpiperazinyl]pyrimidinyl]ethanol III, showed better than the targeted potency with ED90 values of 1-2 mg/kg/day. III was further profiled and found to be a selective inhibitor of sorbitol dehydrogenase, with excellent pharmacodynamic/pharmacokinetic properties, demonstrating normalization of sciatic nerve fructose in a chronically diabetic rat model for .apprx.17 h, when administered orally at a single dose of 2 mg/kg/day.

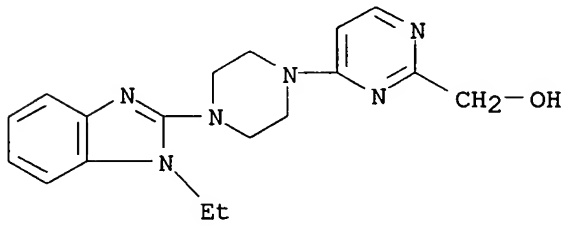
IT **400785-12-8P 400785-22-0P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and structure-activity relationships of oral antidiabetic, sorbitol dehydrogenase-inhibiting heterocyclic piperazinopyrimidines)

RN 400785-12-8 CAPLUS

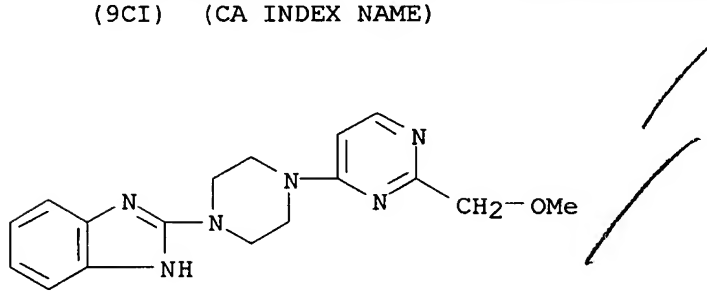
CN 2-Pyrimidinemethanol, 4-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



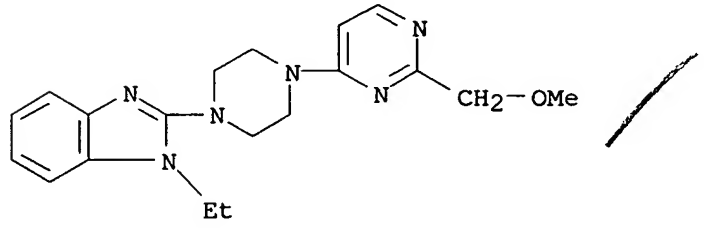
RN 400785-22-0 CAPLUS
CN 2-Pyrimidinemethanol, 4-[4-(1-ethyl-1H-benzimidazol-2-yl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



IT **400785-04-8P 400785-05-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and structure-activity relationships of oral antidiabetic, sorbitol dehydrogenase-inhibiting heterocyclic piperazinopyrimidines)
RN 400785-04-8 CAPLUS
CN 1H-Benzimidazole, 2-[4-[2-(methoxymethyl)-4-pyrimidinyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 400785-05-9 CAPLUS
CN 1H-Benzimidazole, 1-ethyl-2-[4-[2-(methoxymethyl)-4-pyrimidinyl]-1-piperazinyl]- (9CI) (CA INDEX NAME)

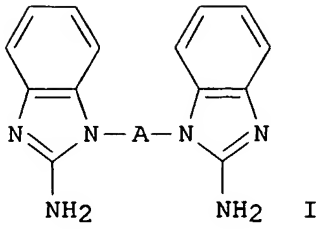


RE.CNT 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 12 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 2000:34861 CAPLUS
DN 132:93320
TI Preparation of aminobenzimidazoles and guanidines as novel potassium channel blocking agents
IN Teuber, Lene; Olesen, Soren-Peter; Strobaek, Dorte; Jensen, Bo Skaaning; Peters, Dan
PA Neurosearch A/S, Den.
SO PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000001676	A1	20000113	WO 1999-DK378	19990701
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9947689	A1	20000124	AU 1999-47689	19990701
	EP 1091942	A1	20010418	EP 1999-931019	19990701
	EP 1091942	B1	20050330		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	JP 2002519412	T2	20020702	JP 2000-558081	19990701
	AT 292120	E	20050415	AT 1999-931019	19990701
	US 6194447	B1	20010227	US 1999-347514	19990702
	US 2002049246	A1	20020425	US 2000-750345	20001229
	US 6380180	B2	20020430		
	US 2002137784	A1	20020926	US 2002-84179	20020228
	US 6569880	B2	20030527		
PRAI	DK 1998-865	A	19980702		
	US 1998-92218P	P	19980708		
	WO 1999-DK378	W	19990701		
	US 1999-347514	A3	19990702		
	US 2000-750345	A3	20001229		

OS MARPAT 132:93320
GI



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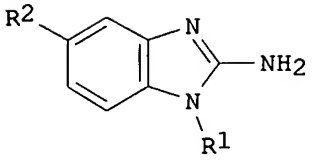
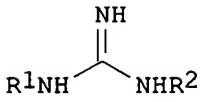


II



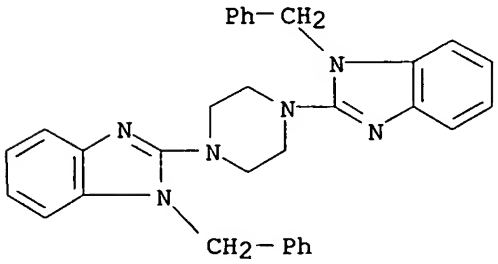
III

AB The title compds. [I (A = a spacing group contg. of 1-20 atoms), II (R1 = mono- or polycyclic (un)substituted aryl, aralkyl, mono- or polycyclic heterocyclyl, etc.; R2 = H, alkyl, CF3), III (R1, R2 = H, alkyl, mono- or polycyclic heterocyclyl, etc.), etc.], useful for the treatment or alleviation of diseases or disorders assocd. with the activity of potassium channels, in particular asthma, cystic fibrosis, chronic obstructive pulmonary disease, convulsions, vascular spasms, coronary artery spasms, renal disorders, etc., were prepd. Thus, treatment of N,N'-bis(2-aminophenyl)-1,4-butanediamine.2HCl (prepn. given) with cyanogen bromide in DMF afforded I [A = (CH)4]. Biol. data for some of the title compds. were given.

IT **254434-82-7P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of aminobenzimidazoles and guanidines as potassium channel blocking agents)

RN 254434-82-7 CAPLUS

CN 1H-Benzimidazole, 2,2'-(1,4-piperazinediyl)bis[1-(phenylmethyl)- (9CI) (CA INDEX NAME)



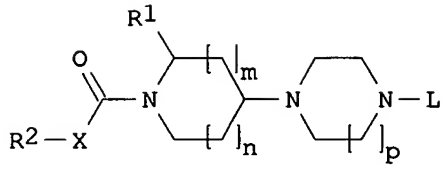
RE.CNT 104 THERE ARE 104 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1997:425258 CAPLUS
DN 127:34245
TI Preparation of 1-(1,2-disubstituted piperidinyl)-4-substituted piperazine derivatives as substance-P antagonists
IN Janssens, Frans Eduard; Sommen, Francois Maria; Surleraux, Dominique Louis Nestor Ghislaine; Leenaerts, Joseph Elisabeth; Van Roosbroeck, Yves Emiel Maria
PA Janssen Pharmaceutica N.V., Belg.; Janssens, Frans Eduard; Sommen, Francois Maria; Surleraux, Dominique Louis Nestor Ghislaine; Leenaerts, Joseph Elisabeth; Van Roosbroeck, Yves Emiel Maria
SO PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9716440	A1	19970509	WO 1996-EP4660	19961025
	W: AL, AM, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, IL, IS, JP, KG, KR, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, TR, TT, UA, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
	TW 460473	B	20011021	TW 1996-85113017	19961024
	CA 2234096	AA	19970509	CA 1996-2234096	19961025
	CA 2234096	C	19970509		
	AU 9674932	A1	19970522	AU 1996-74932	19961025
	AU 704155	B2	19990415		
	EP 862566	A1	19980909	EP 1996-937248	19961025
	EP 862566	B1	20000112		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
	CN 1205699	A	19990120	CN 1996-199225	19961025
	CN 1117744	B	20030813		
	BR 9611184	A	19990330	BR 1996-11184	19961025
	JP 11514634	T2	19991214	JP 1997-517050	19961025
	JP 3073238	B2	20000807		
	AT 188691	E	20000115	AT 1996-937248	19961025
	ES 2143238	T3	20000501	ES 1996-937248	19961025
	PT 862566	T	20000630	PT 1996-937248	19961025
	IL 123962	A1	20010111	IL 1996-123962	19961025
	PL 185029	B1	20030228	PL 1996-327406	19961025
	CZ 291794	B6	20030514	CZ 1998-1322	19961025
	ZA 9609090	A	19980429	ZA 1996-9090	19961029
	HR 960507	B1	20010831	HR 1996-960507	19961030
	NO 9801534	A	19980624	NO 1998-1534	19980403
	NO 310232	B1	20010611		
	US 6197772	B1	20010306	US 1998-54963	19980403
	GR 3033154	T3	20000831	GR 2000-400847	20000404
	US 6521621	B1	20030218	US 2000-745513	20001222
	US 37886	E	20021015	US 2001-935698	20010823
	CN 1438220	A	20030827	CN 2002-157427	20021217
PRAI	EP 1995-202929	A	19951030		
	EP 1996-937248	A	19961025		
	WO 1996-EP4660	W	19961025		
	US 1998-54963	A1	19980403		

OS MARPAT 127:34245
GI



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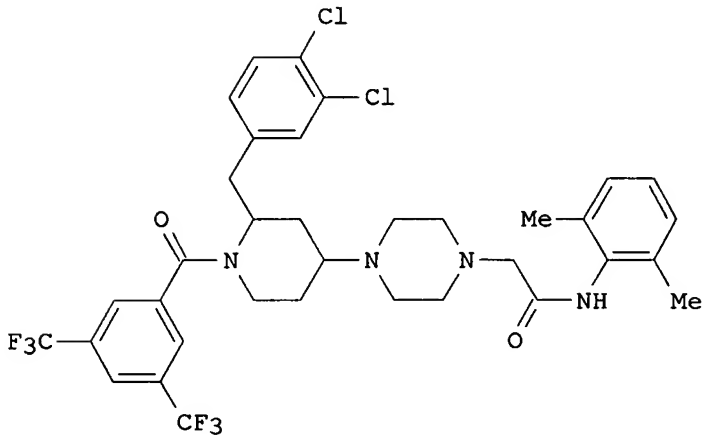


II

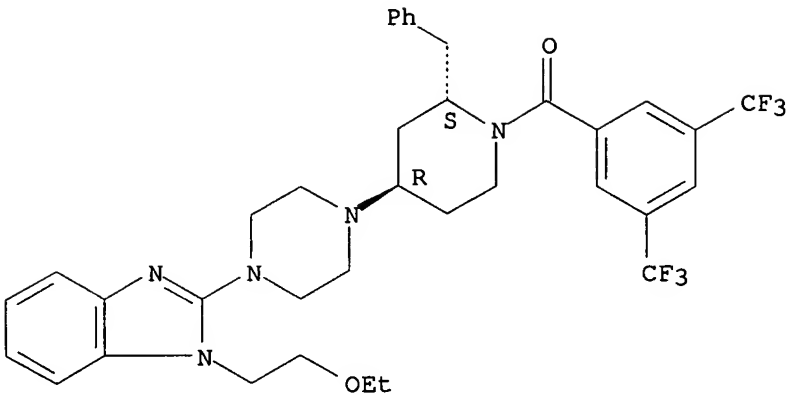
AB The title compds. [I; n = 0-2; m = 1-2 (if m = 2, then n = 1); p = 1-2; Q = O, NR3; X = a covalent bond, a bivalent radical of formula O, S, NR3; R1 = Ar1, Ar1C1-6alkyl, di(Ar1)C1-6alkyl (wherein each C1-6alkyl group is optionally substituted with hydroxy, C1-4alkyloxy, oxo, a ketalized oxo substituent); R2 = Ar2, Ar2C1-6alkyl, Het1, Het1C1-6alkyl; R3 = H, C1-6alkyl; L = H; Ar3; C1-6alkyl, etc.Ar1, Ar2, Ar3 = (un)substituted Ph; Het1, Het2 = monocyclic, bicyclic heterocycle] and their N-oxide forms, the pharmaceutically acceptable addn. salts and the stereoisomeric forms, useful as substance-P antagonists were prepd. and formulated. Thus, reaction of 3,5-bis(trifluoromethyl)benzoyl chloride with (.+-.)-trans-4-{2-[(3,4-dichlorophenyl)methyl]-4-piperidinyl}-N-(2,6-dimethylphenyl)-1-piperazineacetamide in the presence of Et3N in DCM afforded 44% II which showed IC50 of 0.13x10-9 M against substance-P induced relaxation of the pig coronary arteries.

IT **190963-35-0P 190963-36-1P 190963-37-2P**
190963-52-1P 190963-74-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of 1-(1,2-disubstituted piperidinyl)-4-substituted piperazine derivs. as substance-P antagonists)

RN 190963-35-0 CAPLUS

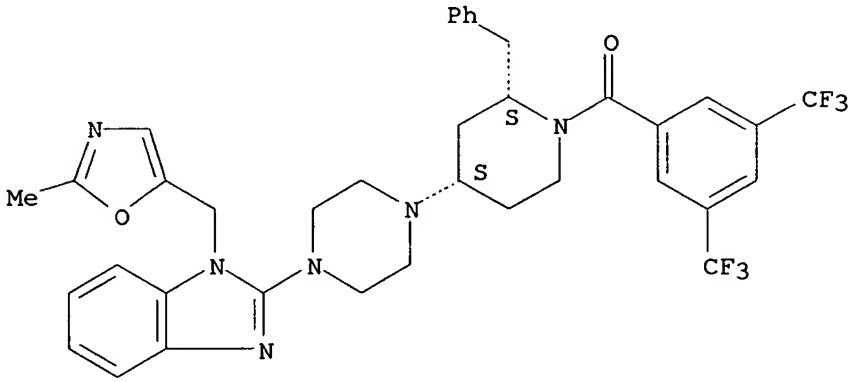
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



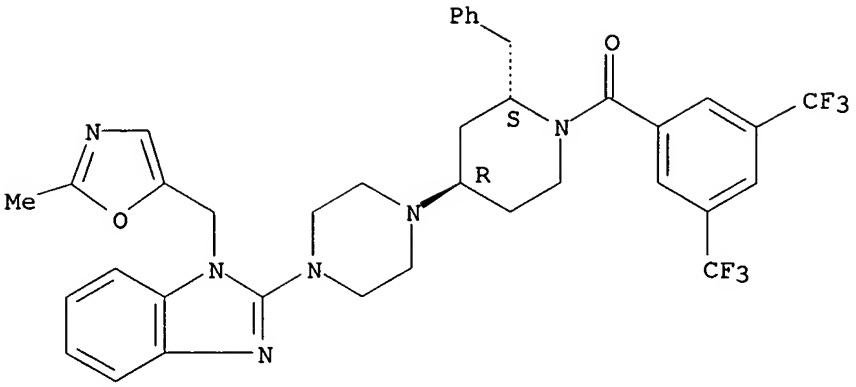
RN 190963-36-1 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-[(2-methyl-5-oxazolyl)methyl]-1H-benzimidazol-2-yl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4R)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



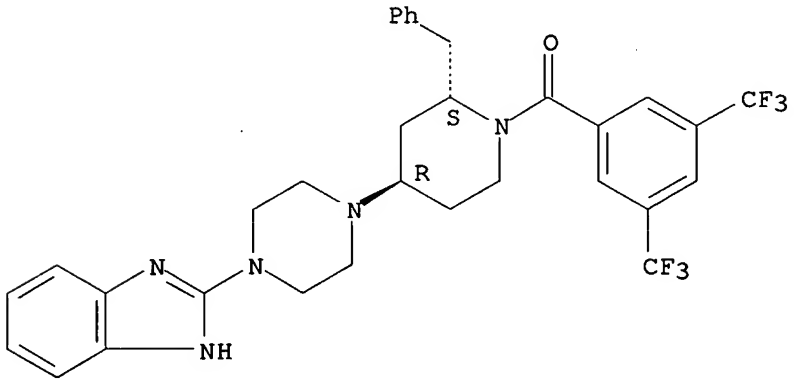
RN 190963-37-2 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-[(2-methyl-5-oxazolyl)methyl]-1H-benzimidazol-2-yl]-1-piperazinyl]-2-(phenylmethyl)-, (2R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.



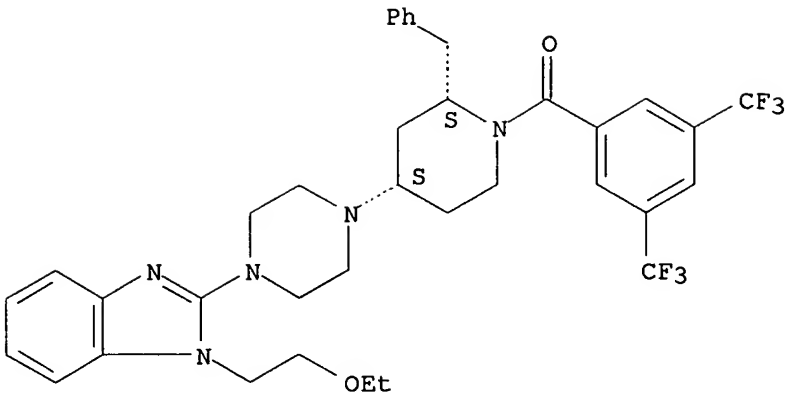
RN 190963-52-1 CAPLUS
CN Piperidine, 4-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-1-[3,5-bis(trifluoromethyl)benzoyl]-2-(phenylmethyl)-, (2R,4S)-rel- (9CI) (CA INDEX NAME)

Relative stereochemistry.

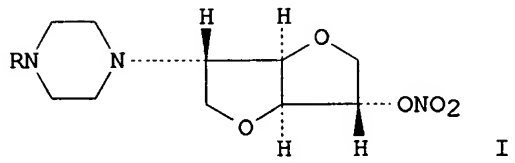


RN 190963-74-7 CAPLUS
CN Piperidine, 1-[3,5-bis(trifluoromethyl)benzoyl]-4-[4-[1-(2-ethoxyethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]-2-(phenylmethyl)-, cis- (9CI) (CA INDEX NAME)

Relative stereochemistry.



L4 ANSWER 14 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1994:218319 CAPLUS
DN 120:218319
TI 1,4:3,6-Dianhydrohexitol nitrate derivatives. II. Synthesis and antianginal activity of aryl- or arylcarbonylpiperazine derivatives
AU Hayashi, Hiroaki; Ikeda, Junichi; Kubo, Kazuhiro; Moriyama, Takahiro; Karasawa, Akira; Suzuki, Fumio
CS Pharm. Res. Lab., Kyotwa Hakko Dogyo Co., Ltd., Nagaizumi, 411, Japan
SO Chemical & Pharmaceutical Bulletin (1993), 41(6), 1100-10
CODEN: CPBTAL; ISSN: 0009-2363
DT Journal
LA English
GI

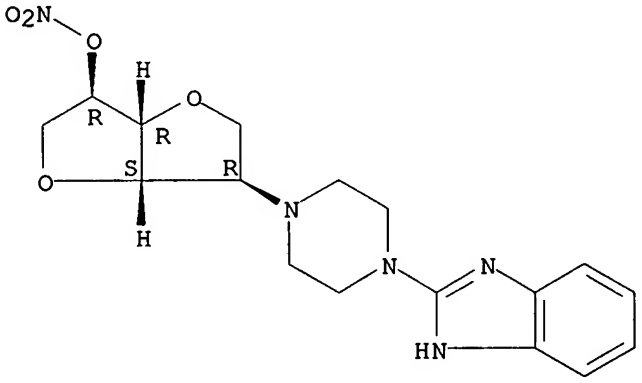


I

AB A series of 5-(4-aryl- or 4-arylcarbonylpiperazin-1-yl)-5-deoxy-1,4:3,6-dianhydro-L-iditol 2-nitrates, I (R = aryl, arylcarbonyl), was prepd. in order to obtain orally active, nitrate-type vasodilators with reduced side effects. The drug design was based on a small redn. in the lipophilicity compared to that of I (R = H) (KF14124). Compds. I [R = benzimidazol-2-yl, nicotinoyl (KW-3196), 3-furoyl] showed potent anti-ischemic activity in a lysine-vasopressin-induced angina pectoris model (rats); their structure-activity relationships are discussed. Compd. KW-3196 exhibited potent vasodilation of the coronary artery in anesthetized dogs and also exhibited potent preload redn. in a heart failure model (dogs) as compared with isosorbide dinitrate, nicorandil, and KF14124. Furthermore, KW-3196 showed much weaker acute lethal toxicity and less central nervous system depression than KF14124 in mice. Thus, KW-3196 is under development as a vasodilator and a drug for treating angina pectoris.
IT **153843-31-3P 153884-79-8P**

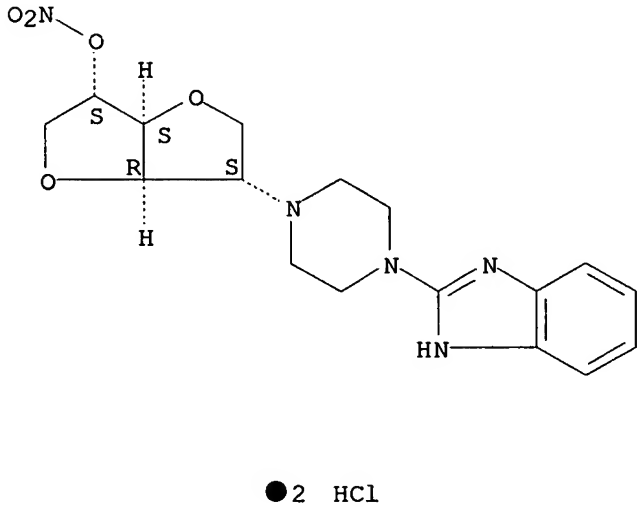
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antianginal activity)
RN 153843-31-3 CAPLUS
CN D-Iditol, 1,4:3,6-dianhydro-2-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-2-deoxy-, 5-nitrate (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 153884-79-8 CAPLUS
CN L-Iditol, 1,4:3,6-dianhydro-2-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-2-deoxy-, 5-nitrate, dihydrochloride (9CI) (CA INDEX NAME)

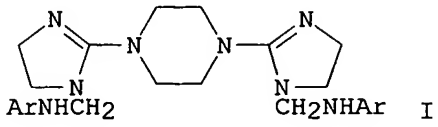
Absolute stereochemistry.



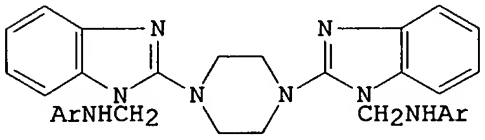
●2 HCl

L4 ANSWER 15 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1992:83632 CAPLUS
DN 116:83632
TI Synthesis and antiparkinsonian activity of 2,2'-(1,4-piperazinediyl)bis[N-(substituted phenyl)-4,5-dihydro-1H-imidazole-1-methanamines] and 2,2'-(1,4-piperazinediyl)bis[N-(substituted phenyl)-1H-benzimidazole-1-methanamines]
AU Naithani, Pankaj K.; Bhalla, Manish; Palit, Gautam; Srivastava, V. K.;

Shankar, K.
CS Dep. Pharmacol. Ther., King George's Med. Coll., Lucknow, 226 003, India
SO Indian Journal of Heterocyclic Chemistry (1991), 1(2), 65-70
CODEN: IJCHEI; ISSN: 0971-1627
DT Journal
LA English
GI

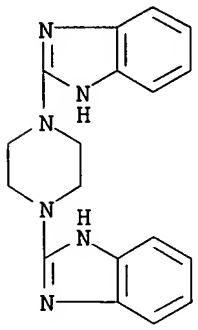


I

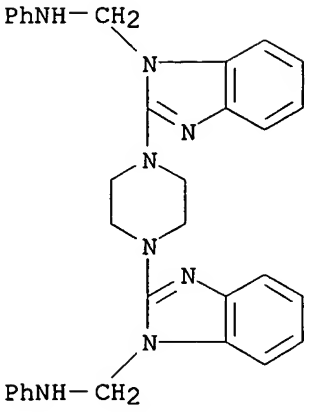


II

AB Piperazines I (Ar = Ph, 2-MeC6H4, 4-ClC6H4, 4-MeOC6H4, 2,5-Cl2C6H3) and II were synthesized in 3 steps from 1,4-dicyanopiperazine and screened for their antiparkinsonian activity and toxicity. I (Ar = 4-ClC6H4), the most active compd., when screened for its dopamine (DA) receptor binding activity, showed affinity for DA receptors.
IT **138768-65-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and Mannich reactions of)
RN 138768-65-7 CAPLUS
CN 1H-Benzimidazole, 2,2'-(1,4-piperazinediyl)bis- (9CI) (CA INDEX NAME)

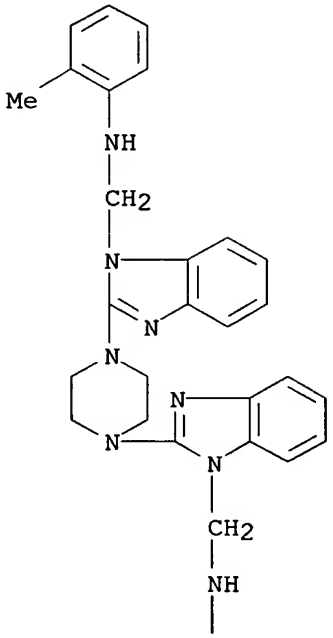


IT **138768-93-1P 138768-94-2P 138768-95-3P**
138768-96-4P 138768-97-5P
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. and antiparkinsonian activity of)
RN 138768-93-1 CAPLUS
CN 1H-Benzimidazole-1-methanamine, 2,2'-(1,4-piperazinediyl)bis[N-phenyl- (9CI) (CA INDEX NAME)

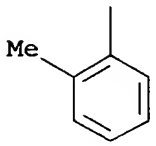


RN 138768-94-2 CAPLUS
CN 1H-Benzimidazole-1-methanamine, 2,2'-(1,4-piperazinediyl)bis[N-(2-methylphenyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

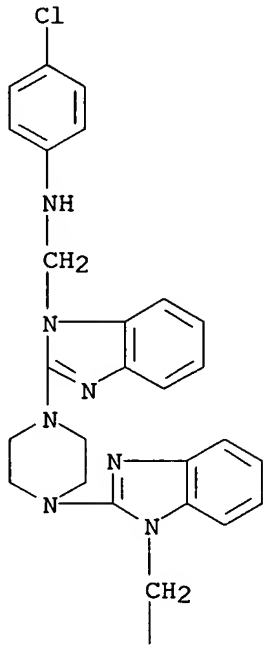


PAGE 2-A

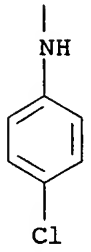


RN 138768-95-3 CAPLUS
CN 1H-Benzimidazole-1-methanamine, 2,2'-(1,4-piperazinediyl)bis[N-(4-chlorophenyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

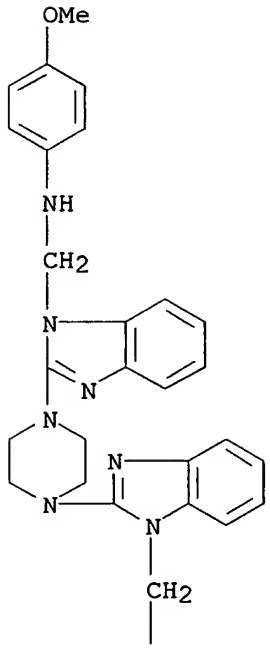


PAGE 2-A

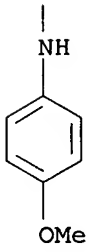


RN 138768-96-4 CAPLUS
CN 1H-Benzimidazole-1-methanamine, 2,2'-(1,4-piperazinediyl)bis[N-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)

PAGE 1-A

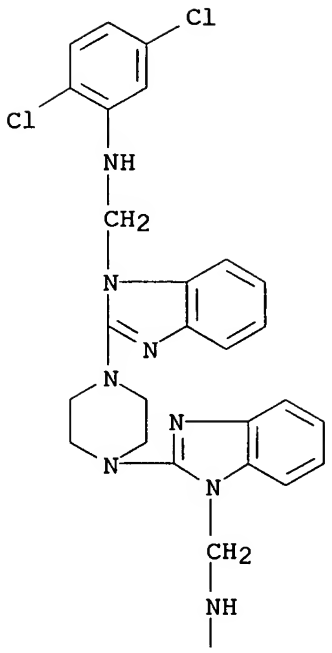


PAGE 2-A

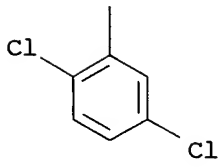


RN 138768-97-5 CAPLUS
CN 1H-Benzimidazole-1-methanamine, 2,2'-(1,4-piperazinediyl)bis[N-(2,5-dichlorophenyl)- (9CI) (CA INDEX NAME)

PAGE 1-A



PAGE 2-A



L4 ANSWER 16 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1991:536644 CAPLUS
DN 115:136644
TI Preparation of heterocyclylhexitols as coronary vasodilators
IN Suzuki, Fumio; Hayashi, Hiroaki; Kuroda, Takeshi; Kubo, Kazuhiro; Ikeda, Junichi
PA Kyowa Hakko Kogyo Co., Ltd., Japan
SO Eur. Pat. Appl., 92 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

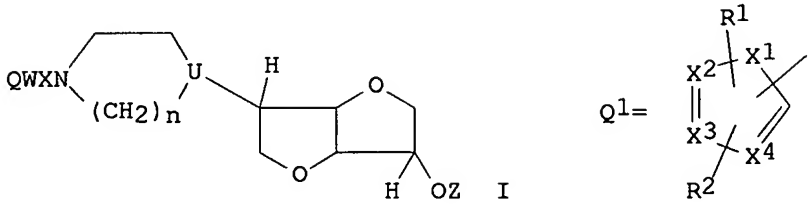
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI EP 393574	A2	19901024	EP 1990-107245	19900417
EP 393574	A3	19910821		
EP 393574	B1	19960131		

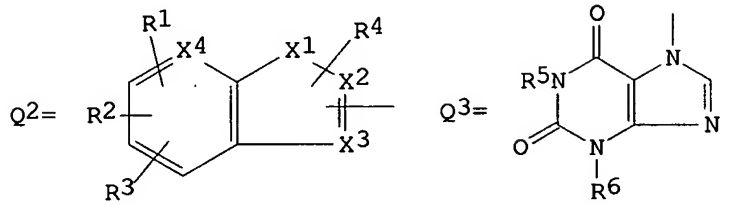
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE

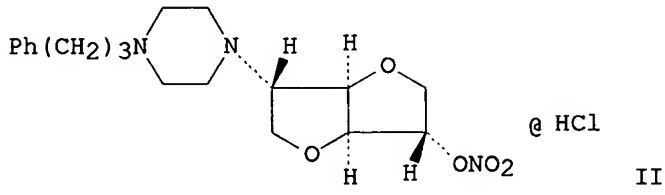
	CA 2014520	AA	19901017	CA 1990-2014520	19900412
	CA 2014520	C	19960716		
	US 5053408	A	19911001	US 1990-508701	19900413
	JP 03218381	A2	19910925	JP 1990-100005	19900416
	JP 2954647	B2	19990927		
	AT 133671	E	19960215	AT 1990-107245	19900417
	ES 2085295	T3	19960601	ES 1990-107245	19900417
PRAI	JP 1989-97032	A	19890417		
	JP 1989-293125	A	19891110		

OS MARPAT 115:136644

GI







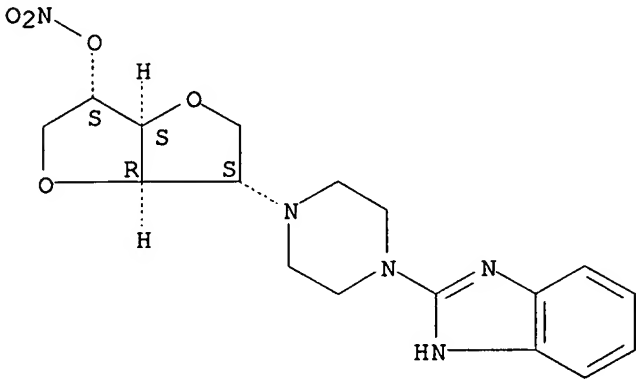
AB Title compds. [I; Q = Q1, Q2, Q3, etc.; X1 = NH, O, S; X2-X4 = CH, N; R1-R4 = H, alkyl, CF3, aryl, alkanoyloxy, amino, alkanoyl, halo, NO2, etc.; R5, R6 = H, alkyl; U = N, N(O); W = bond, O, S; X = (CY1Y2)l, CY3:CY4 = (CY1Y2)l; Y1, Y2 = H, alkyl, OH, alkanoyloxy, cyano, Ph; Y1Y2 = O; Y3, Y4 = H, alkyl; l = 0-6; Z = H, NO2; n = 2, 3], were prepd. Thus, a mixt. of 1,4:3,6-dianhydro-D-glucitol 5-methanesulfonate was refluxed 36 h with piperazine in BuOH to give 5-deoxy-5-piperazin-1-yl-1,4:3,6-dianhydro-L-iditol methanesulfonate. The latter in aq. H2SO4 was added to a -15.degree. mixt. of urea and 86% HNO3 in conc. H2SO4 to give 38% 5-deoxy-5-piperazin-1-yl-1,4:3,6-dianhydro-L-iditol 2-nitrate. The latter was refluxed 24 h with 1-chloro-3-phenylthiopropane and Et3N in EtOH to give 34% of title compd. II. II at 0.3 mg/kg i.d. was effective against propranolol-induced heart failure in dogs.

IT **134186-00-8P 134186-41-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of, as coronary vasodilator)

RN 134186-00-8 CAPLUS

CN L-Iditol, 1,4:3,6-dianhydro-2-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-2-deoxy-, 5-nitrate, hydrochloride (9CI) (CA INDEX NAME)

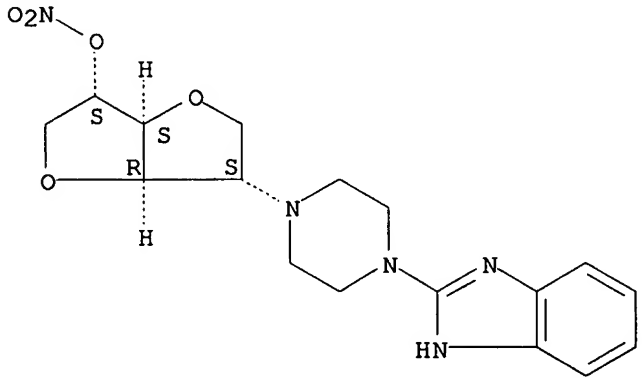
Absolute stereochemistry.



●x HCl

RN 134186-41-7 CAPLUS
CN L-Iditol, 1,4:3,6-dianhydro-2-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-2-deoxy-, 5-nitrate (9CI) (CA INDEX NAME)

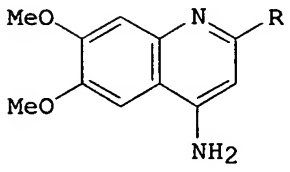
Absolute stereochemistry.



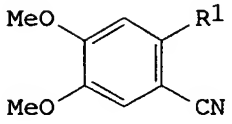
L4 ANSWER 17 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1984:407051 CAPLUS
DN 101:7051
TI 2-Substituted 4-amino-6,7-dimethoxyquinolines
IN Campbell, Simon Fraser; Hardstone, John David
PA Pfizer Ltd., UK; Pfizer Corp.
SO Eur. Pat. Appl., 51 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 100200	A1	19840208	EP 1983-304196	19830720
	EP 100200	B1	19870506		
	R: AT, BE, CH, DE, FR, GB, IT, LI, LU, NL, SE				
	US 4656174	A	19870407	US 1983-515095	19830719
	AT 26978	E	19870515	AT 1983-304196	19830720
	FI 8302658	A	19840125	FI 1983-2658	19830721
	FI 78296	B	19890331		
	FI 78296	C	19890710		
	ES 524320	A1	19850416	ES 1983-524320	19830721
	PL 139498	B1	19870131	PL 1983-243131	19830721
	DK 8303373	A	19840125	DK 1983-3373	19830722
	DK 166821	B1	19930719		
	NO 8302688	A	19840125	NO 1983-2688	19830722
	NO 171594	B	19921228		
	NO 171594	C	19930407		
	AU 8317222	A1	19840126	AU 1983-17222	19830722
	AU 548036	B2	19851121		
	JP 59033264	A2	19840223	JP 1983-134244	19830722
	JP 02019112	B4	19900427		
	HU 31688	O	19840528	HU 1983-2594	19830722
	HU 190907	B	19861228		
	ZA 8305355	A	19840530	ZA 1983-5355	19830722
	DD 211555	A5	19840718	DD 1983-253330	19830722
	SU 1251801	A3	19860815	SU 1983-3618703	19830722
	CS 247073	B2	19861113	CS 1983-5509	19830722
	IL 69311	A1	19870130	IL 1983-69311	19830722
	CA 1255670	A1	19890613	CA 1983-433023	19830722
	SU 1340589	A3	19870923	SU 1984-3732816	19840426
	US 4686228	A	19870811	US 1986-925029	19861030
	US 4758568	A	19880719	US 1987-48343	19870511
	NO 9003181	A	19840125	NO 1990-3181	19900717
	NO 173605	B	19930927		
	NO 173605	C	19940105		
PRAI	GB 1982-21457	A	19820724		
	US 1983-515095	A3	19830719		
	EP 1983-304196	A	19830720		
	NO 1983-2688	A1	19830722		
	US 1986-925029	A3	19861030		
OS	MARPAT 101:7051				

GI



I



II

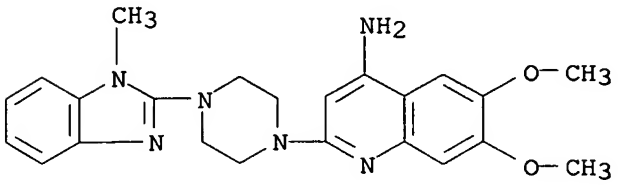
AB Antihypertensive (no data) aminodimethoxyquinolines I (R = tertiary amino) were prepd. Thus the aniline II (R1 = NH2) was treated with MeC(OEt)3 to give II (R1 = N:CMeOEt) which was treated with N-benzylpiperazine to give II [R1 = 1-(4-benzylpiperazino)ethylideneamino, III]. Cyclization of III with ZnCl2 gave I (R = 4-benzylpiperazino) which was hydrogenolyzed to I

(R = piperazino). Acylation of I (R = piperazino) with 1,4-benzodioxan-2-carbonyl chloride gave I [R = 4-(1,4-benzodioxan-2-ylcarbonyl)piperazino].

IT **90402-23-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

RN 90402-23-6 CAPLUS

CN 4-Quinolinamine, 6,7-dimethoxy-2-[4-(1-methyl-1H-benzimidazol-2-yl)-1-piperazinyl]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

L4 ANSWER 18 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN

AN 1983:34596 CAPLUS

DN 98:34596

TI 2-(Piperazinyl)-4-pyrimidinamines

IN Rakhit, Sumanas; Bagli, Jehan F.

PA American Home Products Corp., USA

SO U.S., 14 pp. Cont.-in-part of U.S. 4,333,937.
CODEN: USXXAM

DT Patent

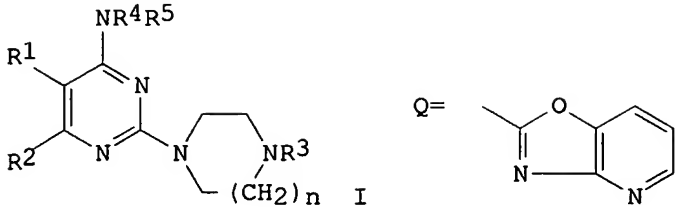
LA English

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 4351832	A	19820928	US 1981-245798	19810320
	US 4333937	A	19820608	US 1980-141548	19800418
	ZA 8102354	A	19821124	ZA 1981-2354	19810408
	CA 1152986	A1	19830830	CA 1981-375300	19810413
	WO 8103022	A1	19811029	WO 1981-US502	19810416
	W: AU, DK, HU, JP, SU				
	RW: AT, CH, DE, FR, GB, LU, NL, SE				
	EP 39190	A1	19811104	EP 1981-301719	19810416
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	AU 8170789	A1	19811110	AU 1981-70789	19810416
	JP 57500561	T2	19820401	JP 1981-501442	19810416
	EP 56027	A1	19820721	EP 1981-901112	19810416
	R: AT, CH, DE, FR, GB, LU, NL, SE				
	DK 8105624	A	19811217	DK 1981-5624	19811217
PRAI	US 1980-141548	A2	19800418		
	US 1981-245798	A	19810320		
	WO 1981-US502	A	19810416		

OS CASREACT 98:34596

GI



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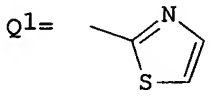
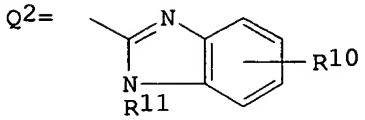
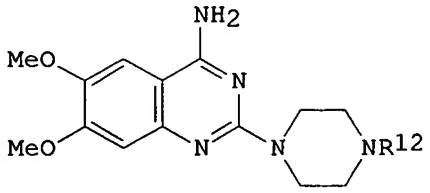






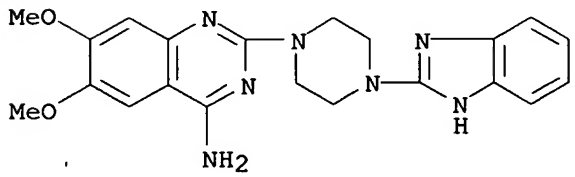
II

AB The antihypertensive (no data) title compds. I [R1,R2 = H, R1R2 = CR6:CR7CR8:CR9 (R6-R9 = H, alkoxy; R3 = Q, Q1, Q2 (R10 = H, halo, alkyl, alkoxy, HO, 1-oxoalkoxy, amino, alkylamino, dialkylamino; R11 = alkyl); R4, R5 = H, alkyl, n = 1, 2] and their therapeutically acceptable and addn. salts were prepd. Thus, 4-amino-6,7-dimethoxy-2-(1-piperazinyl)quinazoline-HCl was treated with 2-chlorobenzimidazole to give the piperazinoquinazolinamine II (R12 = 2-benzimidazolyl). 2-Piperazinocycloheptimidazole-HCl prepd. from methoxy-2,4,6-cyclohexatatriene, was treated with 2-chloro-4-amino-6,7-dimethoxyquinazoline to give II (R12 = 2-cycloheptimidazolyl).

IT **80841-32-3P 80841-34-5P 80841-36-7P 80841-37-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)

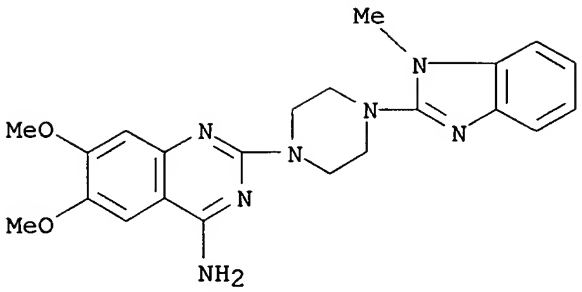
RN 80841-32-3 CAPLUS

CN 4-Quinazolinamine, 2-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-6,7-dimethoxy- (9CI) (CA INDEX NAME)

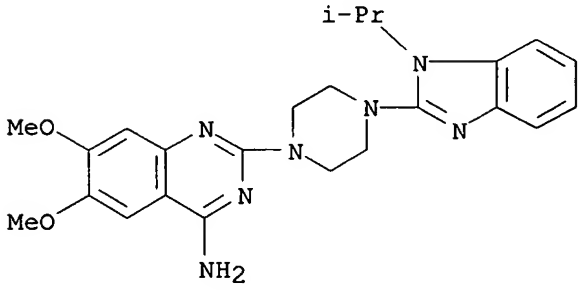


RN 80841-34-5 CAPLUS

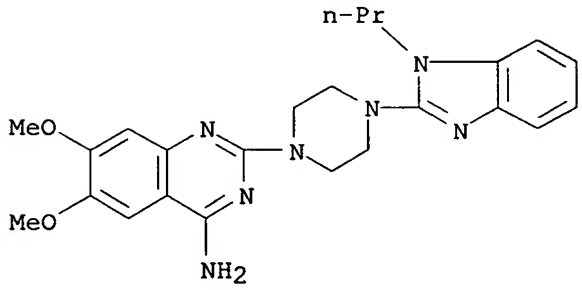
CN 4-Quinazolinamine, 6,7-dimethoxy-2-[4-(1-methyl-1H-benzimidazol-2-yl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 80841-36-7 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-2-[4-[1-(1-methylethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 80841-37-8 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-2-[4-(1-propyl-1H-benzimidazol-2-yl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 19 OF 19 CAPLUS COPYRIGHT 2006 ACS on STN
AN 1982:85588 CAPLUS
DN 96:85588
TI 2-(1-Piperazinyl)-4-pyrimidinamines and related compounds
IN Rakhit, Sumanas; Bagli, Jehan Framroz
PA American Home Products Corp., USA
SO Eur. Pat. Appl., 41 pp.
CODEN: EPXXDW
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 39190	A1	19811104	EP 1981-301719	19810416
	R: AT, BE, CH, DE, FR, GB, IT, LU, NL, SE				
	US 4333937	A	19820608	US 1980-141548	19800418
	US 4351832	A	19820928	US 1981-245798	19810320
	AU 8170789	A1	19811110	AU 1981-70789	19810416
	JP 57500561	T2	19820401	JP 1981-501442	19810416
	DK 8105624	A	19811217	DK 1981-5624	19811217
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OS CASREACT 96:85588

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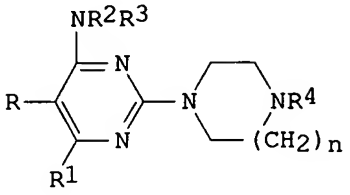

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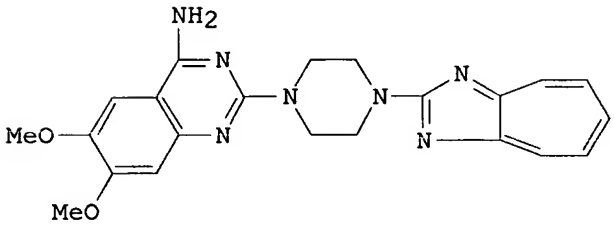


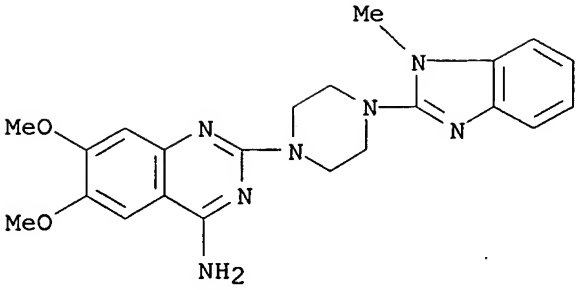
III

AB The title compds. I [R, R1 = H; RR1 = (un)substituted CH:CHCH:CH; R2,R3 = H, alkyl, R4 = (un)substituted pyridooxazolyl,thiazolyl, cycloheptaimidazolyl, oxocycloheptyl, benzoxazolyl, benzothiazolyl, benzimidazolyl; n = 1,2] were prepd. Thus, 2-(1-piperazinyl)cycloheptimidazole (II) was prepd. by treating formylpiperazine with MeSC(:NH)NH2 and 2-methoxy-2,4,6-cycloheptatrienone, followed by deformylation. Treatment of II with 4-amino-2-chloro-6,7-dimethoxyquinazoline gave III, which at 1 mg/kg orally in rats gave a 20% decrease in blood pressure.

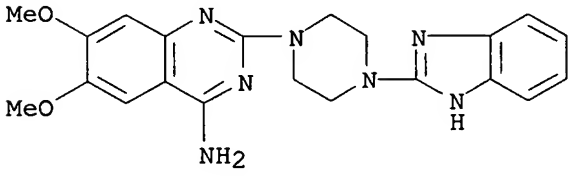
IT **80841-34-5P**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. and antihypertensive activity of)

RN 80841-34-5 CAPLUS

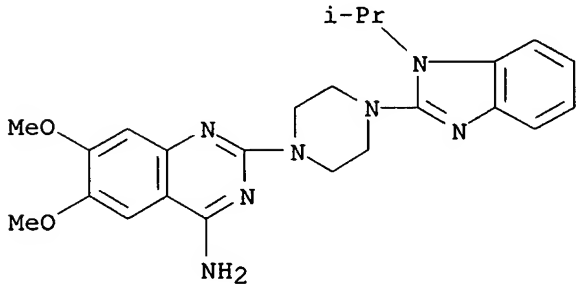
CN 4-Quinazolinamine, 6,7-dimethoxy-2-[4-(1-methyl-1H-benzimidazol-2-yl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



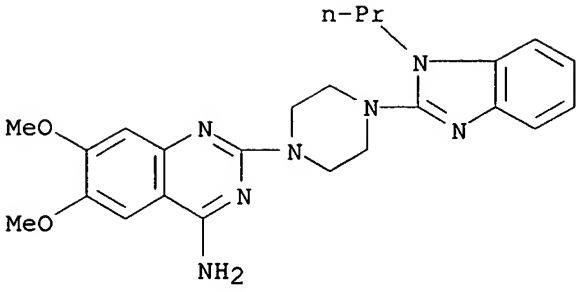
IT **80841-32-3P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. and methylation of)
RN 80841-32-3 CAPLUS
CN 4-Quinazolinamine, 2-[4-(1H-benzimidazol-2-yl)-1-piperazinyl]-6,7-dimethoxy- (9CI) (CA INDEX NAME)



IT **80841-36-7P 80841-37-8P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 80841-36-7 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-2-[4-[1-(1-methylethyl)-1H-benzimidazol-2-yl]-1-piperazinyl]- (9CI) (CA INDEX NAME)



RN 80841-37-8 CAPLUS
CN 4-Quinazolinamine, 6,7-dimethoxy-2-[4-(1-propyl-1H-benzimidazol-2-yl)-1-piperazinyl]- (9CI) (CA INDEX NAME)



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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	66.89	372.42

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-9.75	-24.00

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 13:09:56 ON 16 FEB 2006